The Journal

OF THE KANSAS MEDICAL SOCIETY

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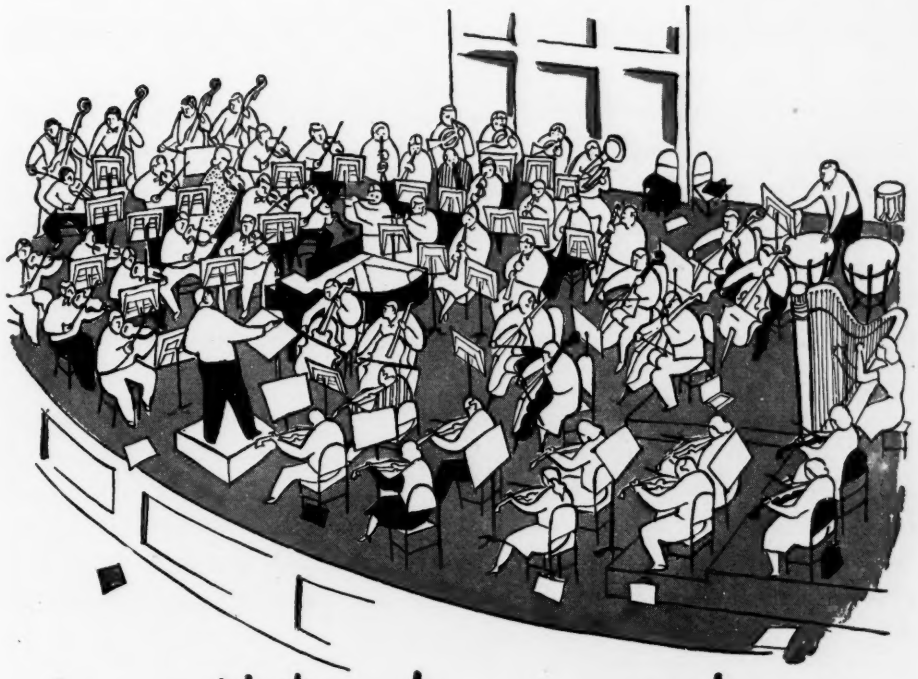

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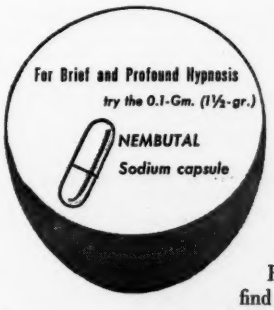

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1. Werner, A.: Acta endocrinol. *13*:87, 1953.
2. Malleson, J.: Lancet *2*:158 (July 25) 1953.
3. Goldzieher, M. A., and Goldzieher, J. W.: Endocrine Treatment in General Practice, New York, Springer Publishing Company, Inc., 1953, p. 21.

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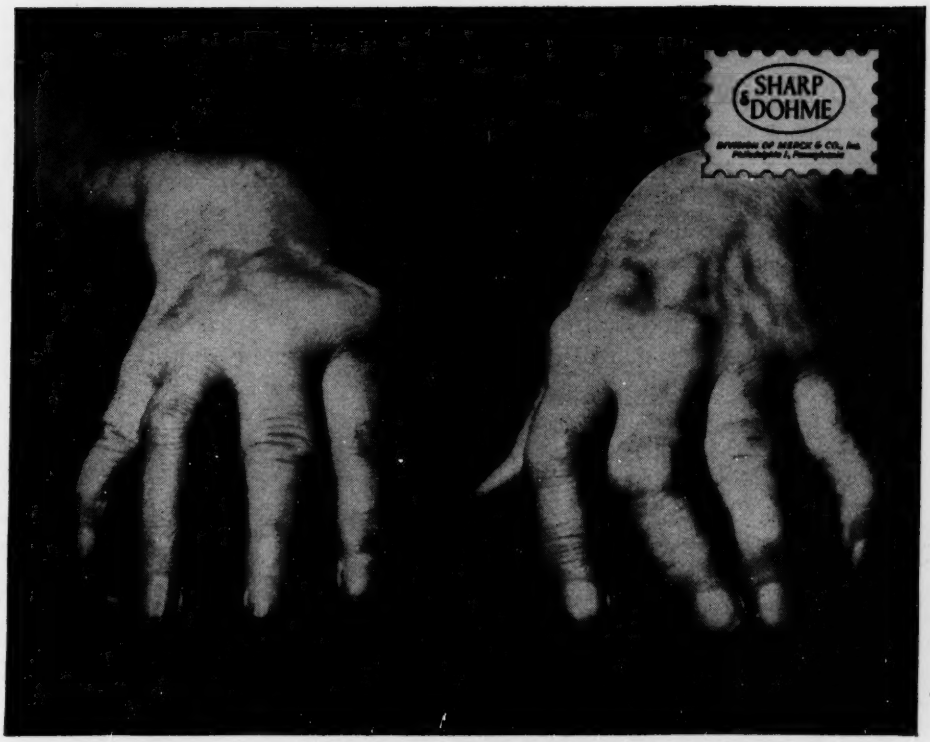

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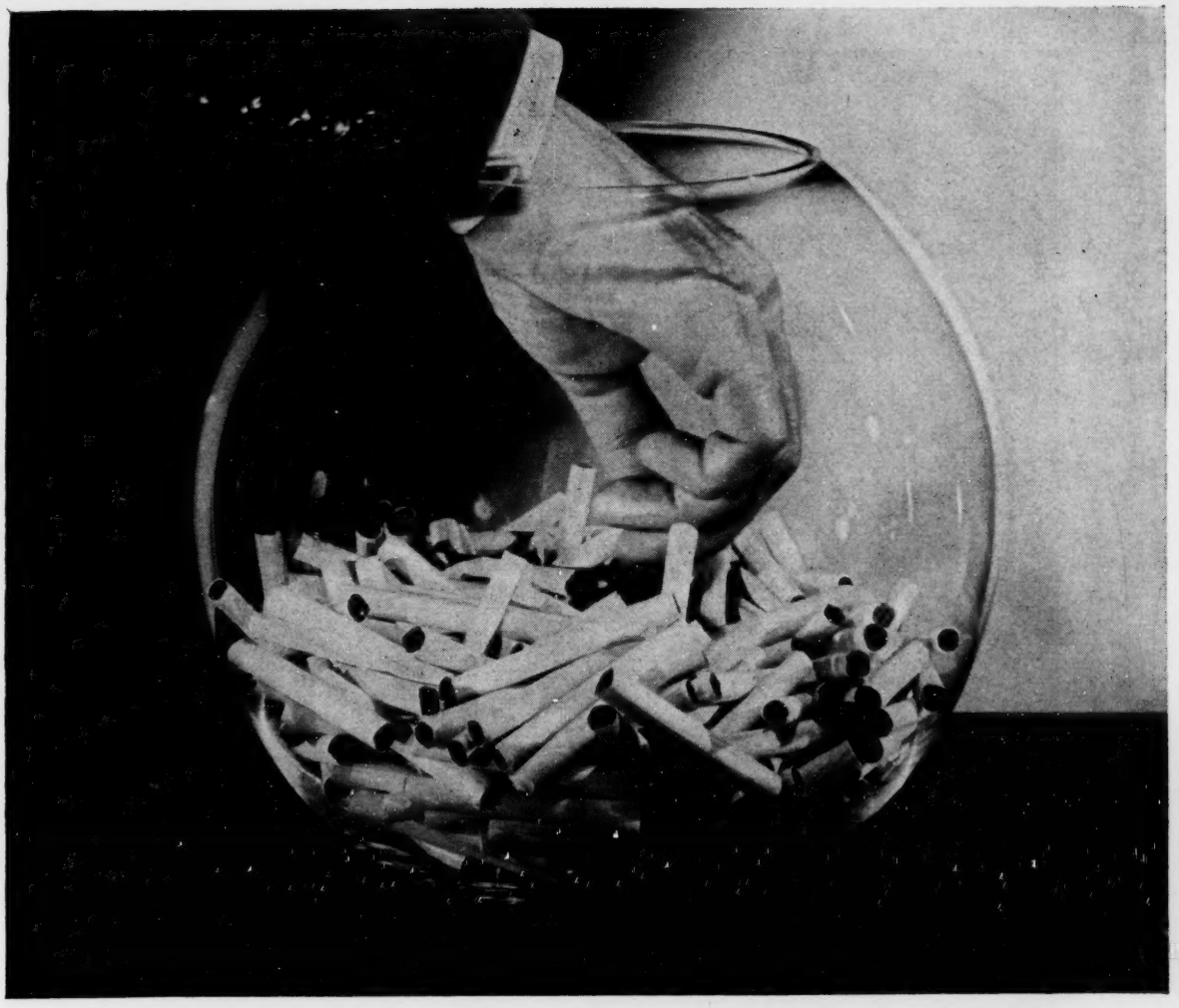

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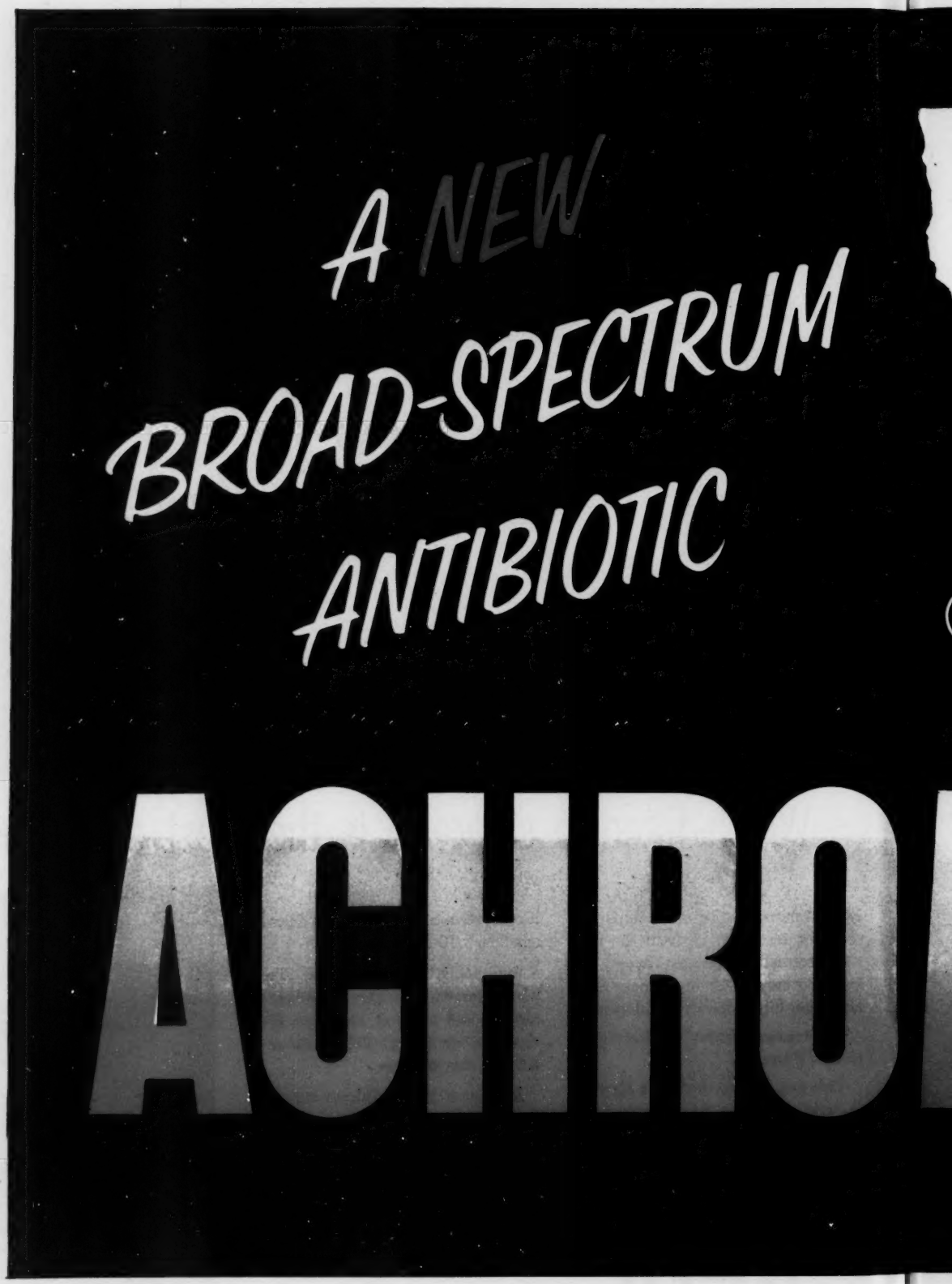
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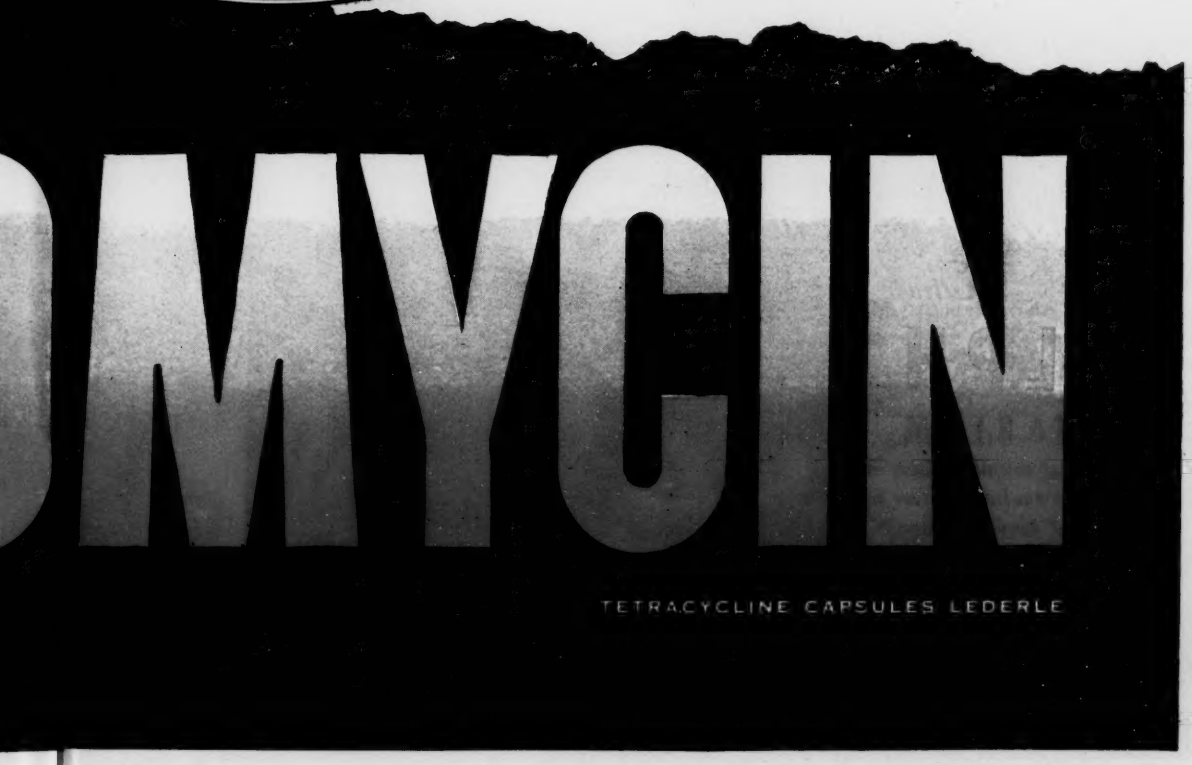

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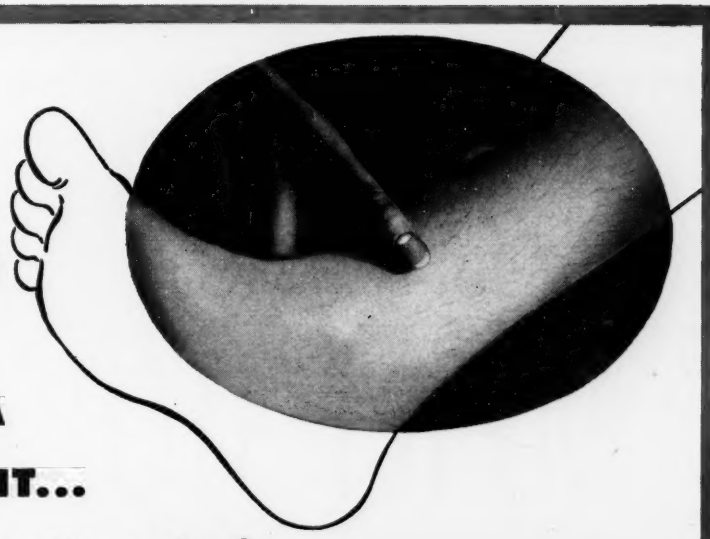

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Volume LV FEBRUARY, 1954 No. 2

Modern Concept of Otitis Media

Harold L. Hickey, M.D.
Denver, Colorado

The title of this presentation might lead some of this audience to believe that the writer is about to regale you with accounts of newly discovered diseases. This, of course, would be impossible as descriptions of otitis media date back to writings of Hippocrates. However, in recent years certain potent factors have modified our thinking and would seem to warrant a studied assessment of ideas and conclusions in the light of new contributions to an old subject. Although acute and chronic otitis media might be considered merely phases of the same condition, it seems profitable to consider them separately.

The pathogenesis of acute otitis media is generally accepted to be the extension of upper respiratory infections, exanthemata, tonsillitis, influenza, so-called virus infections, etc., via the eustachian tube to the middle ear. Anatomical differences in the tube between children and adults favor a greater incidence in the former. Streptococcus hemolyticus still holds first place in bacteriology, but staphylococcic, pneumococcic, and influenzal infections are not uncommon, while Friedlander bacillus and Klebs-Loeffler are rather rare.

The symptoms of otalgia, conduction deafness, fever, leucocytosis, and varying prostration are well known. Local redness of the tympanic membrane, obliteration of land marks, bulging, or even spontaneous rupture with purulent drainage may occur within a few hours of onset. Clinicians (especially otologists) should know that periauricular and mastoid tenderness often seen early is merely part of the invasive stage and not due to mastoiditis. It usually disappears with adequate drainage.

All of the above sounds familar, but now the picture changes. Incident to the universal use of antibiotics or chemotherapy, the fulminating febrile stage appears controlled; and, unless we are alert, subsequent events may go unnoticed. The majority of pediatricians and general practitioners, yes even otologists, are lulled into a sense of satisfaction that the disease is cured merely because sufficient time and effort are not put forth to study in detail the ears and nose. A careful history and follow-up of these patients is also essential.

Meticulous cleansing of the auditory canal and inspection of the membrana tympani, even when drainage is not present or has ceased during the dramatic antibiotic blitz, may reveal a dull, lusterless but not inflamed membrane, hearing subnormal, and mobility impaired when checked with the Siegel pneumatic scope. Infections in the nose or sinuses, enlarged adenoid masses even after tonsil and adenoid operations, may contribute to the failure of resolution. However, probably the most common error is the failure to establish drainage by myringotomy in the acute stage as we would have done years ago. It is a cardinal principle of good surgery that infections require drainage, and the galaxy of modern drugs, wonderful as they are, has not changed that principle.

Patients, especially children, frequently present recurrent attacks which are interpreted as new infections when more than likely the original infection was not completely controlled due to discontinuation of medication too soon or failure to perform myringotomy when it was needed.

It is becoming standard procedure in most of the city and town schools, as well as in many rural areas, to make periodic hearing tests by audiometer. While

Presented before the Eye, Ear, Nose and Throat Section of the Kansas Medical Society, May 6, 1953.

this is only a screening test which should lead the patient to the otologist, its value cannot be questioned. It is my opinion that many of the hearing defects thus discovered might have been prevented by adequate care of acute otitis media.

From the above remarks I would not care to leave the impression that every case of acute otitis media requires myringotomy, but it is a statistical fact that mastoiditis occurs in a higher percentage of patients in whom the drum ruptures spontaneously. Also, not all patients require antibiotics or chemotherapy. Nasal shrinkage to encourage ventilation of the middle ear, having the patient rest with the involved ear uppermost, management of allergies, and instruction as to nose blowing all have a bearing on the outcome of the acute ear.

Contrary to popular belief, simple mastoidectomy is still necessary in the management of some of the neglected and ill treated cases; however, incidence is so much lower that it is becoming difficult for residents in otolaryngology to have adequate training in performing the operation. I still perfer the postauricular approach for simple mastoidectomy as it offers a better opportunity, for me at least, to manage extensions of the suppurative process. Many of us have seen ears with mastoids successfully operated upon but with partially stenosed auditory canals and severely depressed scars. With a little care in technique at operation and adequate postoperative packing of the canal, such results can be avoided.

It should be pointed out that, due to antibiotic suppression, mastoid infection may develop and progress almost to complete breakdown without alarming symptoms. It may develop without pain, fever, or increased white count. Failure of the tympanic membrane to return to normal and the lack of complete restoration of good hearing should excite suspicion. Unfortunately, a child in school does not always report decreased hearing, but an alert teacher or parent may detect it.

Lack of adequate treatment encourages chronicity, and this is especially true in the case of a spontaneous rupture of the tympanic membrane in Shrapnell's area. The chronic ear will be more fully discussed later.

There is a condition which occupies a middle ground between acute and chronic otitis media and about which much has been said and written. I refer to otitis media with effusion, secretory otitis media, hydrops of the middle ear, aerotitis media, nonsuppurative or catarrhal otitis media. The particular terminology is not important as long as we understand the mechanism of its occurrence and recognize the symptoms. In my personal experience, it has been a disease of adults more frequently than of children. An airplane trip during an upper respiratory infection, especially in a non-pressurized plane, is a common etiologic incident. In the presence of a blocked eustachian tube, equalization of external and intratympanic pressure is impossible, a negative pressure in the middle ear causes pain and, in many cases, the pouring out of fluid of a serous type. The result is rather sudden conductive deafness. The patient may describe a sensation of shifting fluid in the ear.

When the condition is sudden and severe enough to cause redness or even hemorrhagic changes in the tympanic membrane, attention is drawn to the condition and proper treatment will probably ensue. However, in those cases of milder barotrauma or symptoms of fullness and slight deafness incident to upper respiratory infection without the airplane factor, diagnosis may not be so apparent. I have listened to many speakers and have read many articles describing the "amber color of the drum," the "chalky appearance of the umbo," the shifting fluid line, and bubbles on inflation, and yet when I am faced with a diagnosis in a suspected case I often fail to find any of the described findings. In the presence of conductive deafness of recent origin and suggestive symptoms as noted by the patient, I have found the most reliable finding to be immobility of the tympanic membrane when viewed through the Siegel scope. One pathognomonic sign is the clearing of the impaired hearing when the head is tilted forward or to the opposite side, only to have the impairment recur when a normal head position is assumed. It is probable that the fluid overlying the round window causes the impairment.

Treatment in years past has been on the conservative side, such as nasal shrinkage, eustachian catherization and inflation, etc., none of which produced results. Only in recent years has it been appreciated that evacuation of the fluid from the middle ear is the answer. This is accomplished either by paracentesis in the posterior inferior quadrant and aspiration of the viscid stringy fluid with a small suction canula, or by needle puncture and withdrawal of the fluid with a small attached syringe. Since the drum is not inflamed, many workers use no anesthesia. However, the average patient is fearful of having his ear "lanced," and I find that the use of a small amount of local topical anesthesia is reassurring and makes for better co-operation.

In cases of short duration, a single aspiration usually suffices, and the patient is delighted with the almost instantaneous relief of pressure and restoration of hearing. In long standing cases which may not have been previously recognized, repeated aspirations may be needed. This is especially true in persons with chronic allergies who have habitually sniffed through the nose forcibly many times a day. The small tympanic opening heals quickly and causes little discomfort.

In considering chronic suppurative otitis media we have a disease which is age old. There are many possible ramifications and complications to consider, but primarily in diagnosis these narrow down to a few important findings. Location of the perforation tells a great deal, and on that basis we may divide our cases into non-dangerous and dangerous types. The central perforation with mucopurulent discharge, usually odorless, is found in patients with intermittent symptoms, invariably subject to exacerbation during a cold. Hearing will be impaired but may be found to be remarkably good if the patient is tested during the dry phase. This is the non-dangerous type.

By contrast, the marginal perforation, especially in Shrapnell's area, or the so-called attic perforation, from which discharge is more or less continuous and malodorous, should be classified as the dangerous type. The drainage may be almost caseous at times, and extraction with ether may show under the microscope cholesterin crystals characteristic of a cholesteatoma. Inasmuch as the pathology centers around the epitympanum as well as the middle ear proper, the ossicular chain will be damaged, and hearing is consistently worse than in the non-dangerous type.

Since either condition is of long standing, x-ray films of the mastoid will show sclerosis and obliteration of most of the pneumatic structure; the anterior wall of the lateral sinus will stand out in sharp contrast. I get more information from a well taken Law position view, but others prefer a Stenver's position. Dr. Gilbert Owen in Los Angeles has devised a special projection which, in his hands, gives a remarkable delineation of the attic, antrum, and even semicircular canals. However, it does not seem to be usable by most other radiologists. In the case of cholesteatoma which is sizable, there will be seen a rarefied area within the sclerotic antrum or along the lateral sinus wall, which is an important aid to diagnosis.

The presence of aural polypi or bleeding granulations protruding through the tympanic perforation also suggests dangerous pathology. Symptoms of temporal headache on the involved side, dizziness, nystagmus, nausea, and vomiting emphasize the seriousness of the condition. Occasionally a sudden facial paralysis may indicate extension of suppuration, and I have seen a few patients who had postponed advised surgery become emergency problems with otitic meningitis or other intracranial complications.

Accurate evaluation of symptoms and signs leads to a diagnosis and determines whether treatment can be conservative and watchful (non-dangerous type) or whether surgery is imperative (dangerous type).

In the conservative treatment, toilet of the ear to keep it clean and dry, and avoidance of swimming and other exposures to water in the ear is important. The patient should realize that prompt care of respiratory infections may avoid recurrent ear attacks. Conservation of hearing is always important, but since some irreparable damage has usually taken place, all we can hope for is to prevent further loss.

For several years at least one author (and perhaps others) has emphasized the importance of chronic antral infection in relation to chronic otitis media, and I am sure we have all noted ipsolateral involvement. Granted that something is gained by proper care, including surgery on the sinus condition, I can hardly accept the glowing reports of cessation of aural drainage, healing of large perforations, and restoration of normal hearing following radical antrum operations.

Local drug therapy has been discussed in a previous paper. In addition to boric alcohol drops when tolerated, or Furacin anhydrous solution, I find many patients benefitted by insufflation of Sulzberger Iodo-bor powder. In cases of central perforations, after they are dry, closure can often be effected by careful use of trichloracetic acid to the edge of the perforation. No attempt should be made to close an upper marginal perforation. If the patient will follow the advice, keeping the involved ear turned upward during sleep will discourage the capillary seepage from the nasopharynx which causes recurrent drainage.

Aural polyps should be removed, using care to avoid snare traction on the pedicle which may be attached to the middle ear promontory. Granulations should be cauterized or removed with a sharp curet or middle ear cupped forceps. Attic irrigations using a small special canula and a dehydrating solution may be tried in those borderline cases which have not shown definite evidence of surgical indications.

One of the problems which I find especially difficult is the decision as to proper treatment, especially surgical, when dealing with an individual with bilateral chronic otitis media. Given a patient with seriously impaired hearing in one ear and continuing evidence of chronic suppuration in the opposite ear, the added social and occupational hazard which would result from a radical operation on the better hearing ear poses a difficult decision. In general, we should be guided by clear indications just as though the patient had a good hearing ear on which to depend.

A few years ago I was forced to perform endaural radical mastoidectomy on both ears in a young man of 17 because of extensive cholesteatoma with impending intracranial involvement. Fortunately, dry ears were secured but with a reduction in hearing bilaterally to loud spoken voice at one foot from the ears. However, he was fitted with a bone conduction

unit (rare in my experience), and he was able to hear ordinary conversation at 20 feet without seeing the speaker's lips. In another case, a school teacher, I debated some time as to a needed radical operation because the opposite ear was not a usable hearing ear. She was operated upon and carries on very successfully, also by the aid of a bone conduction unit.

Having made a diagnosis of chronic suppurative otitis media of the dangerous type which appears to demand operation, both in an attempt to stop the suppuration and to obviate the probability of intracranial extension, in other words to make it a safe ear, how should we approach it? The writer has been in practice long enough to pass through the period when both simple and radical operations were relatively common. His early training and experience were in the post-auricular approach. However, when one has become accustomed to the endaural approach and realizes the many advantages to the operator, the patient, and the ever present need to reduce hospitalization time, I feel sure that he would never wish to return to the post-auricular method for modified radical or complete radical mastoidectomy. The work of Lempert, Meltzer, House, and many others is familiar to most of you, and, if you are not now using the endaural approach, I highly recommend that you take steps in preparation to do so.

Detailed description of the surgical technique of endaural mastoidectomy would serve no useful purpose at this time, but since the operative field is a highly specialized one intimately related to such vulnerable structures as the facial nerve, horizontal semicircular canal, middle fossa dura, oval and round windows, it should be apparent that only a well trained otologist should attempt the operation. Immediate skin grafting of the middle ear and radical cavity encourages more rapid healing, but this is not absolutely necessary. The purpose of the operation, of course, is to remove diseased bone and inflammatory tissue, at the same time converting the mastoid antrum, epitympanum, middle ear, and auditory canal into one cavity accessible to observation and aftercare; thus, the causative pathology is eliminated and intracranial extension is prevented.

SUMMARY AND CONCLUSIONS

Acute and chronic otitis media including otitis media with effusion have been discussed in the light of modern thinking and trends in therapy. Certain pitfalls incident to antibiotic treatment of the acute ear have been noted, and the need for myringotomy has been emphasized. In the surgical management of chronic otitic suppuration, the modern, more direct approach by endaural mastoidectomy offers greater safety and shorter patient convalescence.

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The Pathology of Ectopic Pregnancy

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I should like to begin this paper with a definition of the term "ectopic pregnancy." In popular usage, this term has become almost synonymous with tubal pregnancy. However, in this paper I shall consider any implantation of a fertilized ovum occurring outside of the uterine cavity as constituting an ectopic pregnancy, a tubal pregnancy being but one type of ectopic pregnancy.

There are several types of ectopic pregnancy, each of which shall be discussed in turn. The types are tubal pregnancy, interstitial pregnancy, intraligamentous pregnancy, ovarian pregnancy, abdominal pregnancy, cervical pregnancy, and pregnancy in a rudimentary uterine horn.

Jarcho,[7] in his analysis of 1,225 cases of ectopic pregnancy of all types, gives the following incidences of the various types in his group of cases: the ovum implanted in the ampulla in 578 cases; the isthmus in 265 cases; the fimbriated extremity in 71 cases; the interstitial portion in 45 cases; the infundibula in 31 cases; the entire tube, including a hematosalpinx that contained products of conception, in 17 cases; the abdomen in 17 cases; the distal half of the tube in 10 cases; the distal two-thirds of the tube in 6 cases; the broad ligament in 5 cases; the entire tube and ovary in 5 cases; the cornu in 5 cases; tubo-ovarian in 2 cases; in a rudimentary horn in 1 case. In 164 cases, the site was either not stated or not proved.

Ectopic pregnancy occurs in approximately one of every 300 pregnancies and makes up approximately 1 to 2.5 per cent of all gynecological hospital admissions. It is most common in pregnancies associated with pelvic abnormalities, and it is more

common in Negroes than in whites, the ratio being 1 in 190 admissions to the hospital for whites and 1 in 130 admissions for Negros in one large group.[21] In this same group, the mortality for whites was .7 per cent and for Negroes, 3.9 per cent.

The causes of ectopic pregnancy are variable, but they may be classified under two main groupings. These are: conditions which prevent or retard the passage of the fertilized ovum into the uterine cavity and conditions which increase the receptivity of an ectopic implantation site to the fertilized ovum. Under the first of these classifications may be listed chronic salpingitis, by causing fusions of the folds of the tubal mucosa with narrowing of the tubal lumen or the formation of blind pouches; congenital and postembryonic developmental abnormalities of the tube, particularly diverticula; accessory ostia and hypoplasia; peritubal adhesions following postabortal or puerperal infection with kinking of the tube and narrowing of the lumen; tumors compressing the tube; previous surgery of the pelvis, particularly with resultant adhesions; and external migration of the ovum with resultant growth of the trophoblastic layer before the uterine cavity is reached. The second classification is predominantly concerned with ectopic endometrial tissue foci, particularly in the tubal mucosa.

I shall now proceed to the mechanisms of and the pathological lesions seen in the different types of ectopic pregnancy. The most common of these types, and therefore the most important to the clinician, is the tubal pregnancy, which I shall consider first.

As the uterus and tubes are genetically from the same origin and composed of the same tissues, the reaction to implantation of the fertilized ovum might be expected to be the same in both these tissues. Physiologically, this is true; however, in the tube the results are pathological from the onset, the organ being anatomically entirely unsuited for implantation or development of the ovum.

Until the time that the ovum begins to burrow into the mucosa, the process of development is identical with that found in normal pregnancy, but after this time, in tubal pregnancy, the conditions encountered by the ovum are entirely different. In the tube, there is little connective tissue stroma and no true decidua forms, although a "decidual reaction," with decidual cells throughout the mucosa, singly or in groups, does occur. At the base of the implantation site, no decidua basalis forms, or the little that does form is rapidly destroyed by the lytic action of the trophoblastic layer. The ovum, after penetrating the mucosa, comes immediately into contact with the inner circular muscular layer of the tube, and by its continuing lytic action, in search of an adequate blood supply and point of attachment, lyses the muscle fibers to such an extent that the tubal wall is irreparably weakened. The vessels eroded are of much larger size than those of the uterine decidua, resulting in hemorrhage rather than a normal blood supply into the intervillous spaces in the process of tubal implantation. This hemorrhage is often so extensive that the villi are disrupted and torn, the ovum capsule is distended and eventually ruptures, with resultant hemorrhage into the tubal lumen—the so-called "tubal abortion."

No decidua capsularis analogous to the uterine form develops, although decidual cells and groups of cells are often found. Mucosa and tubular folds can be demonstrated in the walls of the ovum sac nearest the tubal lumen, however, proving its "capsular" nature. This capsule is extremely weak, does not expand and grow with the ovum like true decidua, and, being constantly eroded by villi, ruptures early and easily.

One rather peculiar finding is the fact that the decidual reaction of the tubal mucosa is more extensive the further one progresses in his examination of the tissues distal to the site of implantation. This is seen in the fimbria, in the peritoneum covering the tube, and has even been observed in the tube opposite to the side of implantation. Thickening of the muscularis is seen at the site of implantation, and, at times, away from the implantation site, although generally the muscularis is modified in these locations only when stretched by the developing ovum.

In describing the termination of ectopic gestation in the tube, the terms "tubal abortion" or "tubal rupture" are used. That these terms are not strictly analogous to uterine abortion is apparent when it is realized that separation of the ovum from its attachment and expulsion by the muscular contractions of the tube do not occur. Although separation may occur and the ovum may be found free in the lumen of the tube, this is regarded as a passive carrying of the ovum into the tube by the pressure changes coincidental with rupture of the capsule, rather than the result of any active process initiated by the tubal musculature. That the ovum is often found protruding through the ostium is not regarded as a result of active expulsion by the tube, but rather as a result of implantation near the fimbriated end of the tube, development and enlargement of the ovum subsequently pushing the structure through the ostium following passive dilatation of the tube toward the fimbriated end.

If compression of the ovum does not result in pathological changes so extensive as to be incompatible with further growth, the extruded ovum may continue to grow, retaining its original tubal implantation site with eventual placental extension over the surface of the broad ligament and other nearby pelvic structures, forming the basis for most

abdominal pregnancies. Most authors believe that the ovum with its containing sacs must remain intact if further development is to occur. However, cases have been reported where only the remnants of the sac are present in the abdomen, usually forming adhesions, with the embryo or fetus completely free in the abdominal cavity.

If implantation occurs nearer the uterine end of the tube, termination will occur by any of three mechanisms—by rupture through the weakened tubular wall into the abdominal cavity; by rupture of the capsule into the tubal lumen; or, rarely, by separation of the ovum and its death, with subsequent hydatiform mole or polyp formation possible. The ovum may be pushed through the fimbriated end of the tube by the hemorrhage that occurs with the rupture, but, again, this is not due to any active participation in the process by the tubal musculature. This hemorrhage, in contradistinction to the mechanism in uterine abortion, is not always accompanied by separation of the ovum, but is due to the rupture of the ovum capsule alone. Rupture into the abdominal cavity may also occur secondary to the erosion of a large vessel by villi, the laceration produced being quite small. However, this may terminate fatally due to the constant blood loss occurring through this laceration.

One factor in tubal implantation that is often unrecognized is the effect occasioned by the physical site of implantation, whether on the "tip" of a mucosal fold, or in the peripheral portion of the tubular lumen in a depression between two folds. The latter is by far the most common site. In the former type, after invasion of the mucosa, the ovum lies in the interior of a fold of mucosa and is surrounded on all sides except at its base by this mucosa, greatly limiting its space for expansion. The latter type, as illustrated before, immediately after penetration of the mucosa, lies directly over the muscular layer of the tube with no lateral limitations to its space for expansion. For this reason, the "tip" implantation rarely remains viable and, if it does, the weakening of the muscular wall of the tube occurs later, with its subsequent rupture, than it does following the implantation in the depression between tubular folds.

During the course of tubal pregnancy, particularly if the ovum continues to develop for three months before termination, the uterus proper undergoes hypertrophy, and its endometrium is converted to a decidua vera by the action of the luteal hormones of the ovary, differing from the reaction seen in the normal pregnant uterus only in less marked development of the spongy layer and a greater abundance of blood spaces just beneath the free surface of the decidua. At termination, the decidua becomes degenerate and usually breaks away in small pieces. However, it may come off intact and represent a decidual cast of the uterine cavity. The vaginal "spotting" seen in many cases of ectopic pregnancy is thought to be due to early degenerative changes in this uterine decidua, involution resulting from constriction of the coiled arteries and sometimes reducing the thickness of the decidua by 50 per cent before massive sloughing occurs.

In interstitial ectopic pregnancy, the sequence of events with regard to the ovum is identical with those seen in tubal ectopic pregnancy. However, due to hypertrophy of the adjacent uterine horn musculature and the subsequent stretching similar to that seen in normal intrauterine pregnancy, the ovum may develop for weeks or even months before rupture occurs. When this rupture does occur, the resulting condition is similar to that seen with a ruptured uterus, severe hemorrhage and shock with death within one hour being a typical picture.

In a small number of cases, when the original site of implantation of the ovum is basiotropic, as described by Lichtenstein, that is, in the portion of the tube where the surface is not covered by peritoneum (within the broad ligament), rupture results in the contents of the gestational sac being extruded into the space formed by the separation of these folds of the broad ligament. This is the most "favorable" variety of rupture and terminates either by death of the ovum and the formation of a broad ligament hematoma or by a further development of pregnancy similar to that seen in "tubal abortion" and known as intraligamentous pregnancy. The favorable prognosis following this type of rupture is due to the hemorrhage being confined by the ligamentous folds and thus, being limited, with eventual resorption of the hematoma.

Ovarian pregnancy, as defined by the four criteria of Spiegelberg, demands that the tube, including the fimbriated end, be intact and distinctly separate from the ovary, that the gestational sac occupy the normal position of the ovary, that the sac be connected with the uterus by the utero-ovarian ligament, and that ovarian tissue be demonstrable in the walls of the sac. Many of the ovarian pregnancies reported in the literature do not conform to these criteria. When the sac is composed partially of tubal and partially of ovarian tissue, the term "tubo-ovarian pregnancy" is employed. These occur only with development of the ovum in a tubo-ovarian cyst, or in a tube whose fimbriated end is adherent to the ovary at the time of fertilization.

Various types of true ovarian pregnancy are recognized. These include the primary ovarian pregnancy in which ovarian tissue forms a complete intact layer around the ovum and its sacs. If rupture occurs, it must rupture through a previously intact layer of ovarian tissue, whether adherent organs or tissues covering this ovarian tissue are ruptured or not. Pri-

mary ovarian pregnancy is the result of fertilization of the ovum in situ in the Graafian follicle after rupture, implantation of the fertilized ovum in the Graafian follicle, or implantation in ovarian tissue other than the Graafian follicle. The other main type is the combined ovarian pregnancy, illustrated by the tubo-ovarian pregnancy previously discussed.

Termination of ovarian pregnancy follows the same pattern as seen in tubal pregnancy: rupture of the capsule followed by death of the ovum, usually accompanied by extensive hemorrhage into the abdominal cavity, or continued viability of the ovum with extension of the placenta over adjacent pelvic structures and the development of a secondary abdominal pregnancy. The changes in the uterus are identical with those seen in tubal pregnancy.

Abdominal pregnancy, in the majority of cases, is secondary to the rupture of the aforementioned types of ectopic pregnancy, with continued viability of the ovum. Usually the ovum, after extrusion into the abdominal cavity, becomes encapsulated and degenerates. Mummification, maceration, or calcareous infiltration (lithopedion formation) may then occur. However, a few cases are reported in the literature that are apparently examples of primary implantation of a fertilized ovum in the abdominal cavity. This condition is thought to occur primarily as a result of external migration of the ovum, with the formation of the trophoblastic layer while the ovum is within the abdominal cavity. It is accompanied by normal tubes and ovaries with no evidence of recent or remote injury to the tubes, the absence of any evidence of a uteroperitoneal fistula, and the implantation on a peritoneal surface, with the ovum young enough to eliminate the possibility of secondary implantation following a primary implantation in the tube.

One of the best examples of this type of implantation was described by Studdiford.[25] A rare form of primary abdominal implantation has been described where the fertilized ovum escaped from the uterine cavity through a defect in the uterine wall caused by the postoperative separation of the uterine wound following a previous cesarean section. It has been demonstrated that the peritoneum undergoes a "decidua-like" reaction in abdominal implantation, similar to that seen in tubal pregnancy. However, some authorities do not accept this finding, others believe that abdominal implantation occurs only at sites of ectopic "endometrial" tissue, while still others do not accept the evidence of ectopic "endometrial" tissue on a peritoneal surface. The entire question is controversial, as seen in a review of the literature.

Cervical pregnancy is regarded by many authors as a form of abortion rather than a true ectopic pregnancy. However, in my definition of ectopic pregnancy, this type must be included. It is characterized by ectopic foci of endometrial tissue in the cervical wall mucosa and is included under the increased receptivity of an ectopic implantation site grouping. As the mucosa of the cervix reacts poorly to the invasive action of the trophoblastic layer of the ovum, it is readily destroyed, and the developing placenta becomes anchored to the muscularis. This form of ectopic pregnancy rarely progresses beyond the 20th week of gestation and is usually terminated surgically because of bleeding.

A rudimentary uterine horn is the result of initial lack of development during fetal life of the middle and lower parts of one of the Müllerian ducts, with resulting failure of the two ducts to coalesce. A rudimentary cornu on one side, attached by a band of fibro-muscular tissue to the lower or middle part of the normal uterus of the other side, is the consequence. The tube and the ovary of the defective side are usually well developed, but only about 20 per cent show communication through a minute canal with the uterus.

Pregnancy in a rudimentary horn develops in one of three ways: fertilization through the minute canal, by transperitoneal migration of a spermatozoön, or by transperitoneal migration of the fertilized ovum. That any of these mechanisms may occur is shown by the location of the corpus luteum in the cases presented in the literature, this structure appearing in either ovary. About 90 per cent of these pregnancies terminate with rupture similar to that seen in interstitial pregnancy, the other 10 per cent continuing to term as a result of uterine tissue hypertrophy in the cornu, although the fetus is almost invariably dead "in utero." I find only one case in the literature where the child survived for more than six hours after delivery, this case showing the child alive and well at 2½ years.[15] This type of ectopic pregnancy shows essentially the same symptoms as an abdominal pregnancy, except that the fetus is enclosed in uterine tissue of anomalous origin within the abdominal cavity.

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Weber-Christian Disease: A Case Report

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Weber-Christian disease, or relapsing, febrile, nodular, nonsuppurative panniculitis, is characterized by recurring crops of inflammatory and necrotic nodules in the panniculus adiposus and is usually accompanied by a febrile reaction. The nodules may be single or multiple, tender or painless, freely movable and from 0.5 cm. to several centimeters in diameter. The lesions as a rule do not suppurate but may become necrotic and liquefy. The lesions most commonly occur on the legs, thighs, arms, or breasts, but may occur any place over the body.

Although the lesions may heal without residuals, usually there is a dimpling due to the fibrotic scarring of the subcutaneous fat. The relapses may be as short as a few weeks or as long as several years.

The disease was originally described in 1891 by Pfeifer. Weber, in 1925, described a case using the term "relapsing nonsuppurative panniculitis," and Christian,[5] in 1928, added the term "febrile" to the name.

As it originally was thought to be a rather benign disease, little attention has been paid to it, and for that reason it probably now passes undiagnosed many times. From the literature, Beerman[2] was able to collect 14 cases with a fatal termination. One was that of Mostofi and Engleman,[12] a 39-year-old Filipino male soldier who, at postmortem, showed lesions involving the adipose tissue of the skin, epicardium, peripancreatic, perirenal, and mesenteric areas.

Shuman[13] has pointed out that there are certain similarities in the histopathology to Whipple's disease, erythema nodosum, adiposis dolorosa, insulin granulomata, and scleroderma. While the lesions occur most frequently in the panniculus, they also occur in adipose tissue elsewhere.

Hallahan and Klein,[9] in their review of the literature, felt that although the etiology of relapsing febrile, nodular, nonsuppurating panniculitis was unknown, many factors were to be considered. The halogen group, especially the iodine and bromine compounds, could produce these lesions; also subcutaneous injections of camphor in oil, insulin, and paraffin would produce this response. No organisms nor filterable viruses could be consistently demonstrated from these lesions. Focal infections, septicemia, tuberculosis, renal failure, dietary deficiency, trauma, impaired fat metabolism, foreign body reaction, and endocrine disturbances have all been associated with but not proved as the causative mechanism of this disease. Friedenberg[8] felt Weber-Christian disease represented an allergic reaction to a variety of noxious stimuli.

The disease has occurred in about every age group, with the youngest a 6-month-old infant female, the oldest a 70-year-old female. Beerman states it is most commonly found in obese women between the ages of 20 to 40. However, the disease in recent years is reported with more equal distribution between males and females, although it had been thought to be more common in the female in the proportion of three to one. The disease has been reported in individuals from a number of countries, namely, the United States, Canada, Hawaii, China, Spain, Germany, Scandinavia, Syria, Britain, South America, the Philippines, and Australia. Johnson and Plice[10] reported a case in a Negro.

The onset of the disease is insidious and without prodromata. The nodules may occur with fever, chills, nausea, and malaise. The lesions may remain

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only a short time or for months. Any of the above symptoms may be absent, either singly or in combinations. The constitutional symptoms may be mild, neither incapacitating the individual nor requiring that he be hospitalized.

Beerman states the differential diagnosis must be made from: 1. subcutaneous fat atrophy, 2. insulin lipodystrophy, 3. hypodermic injections and drug addiction, 4. trauma, 5. erythema nodosum, 6. erythema induration, 7. sarcoid of Darier-Roussey, 8. dermatomyositis, 9. morphea, 10. adiposis dolorosa, 11. subcutaneous fat necrosis in the newborn, 12. benign nodular hypodermite, 13. thrombophlebitis, 14. nodular syphilis, 15. leprosy, 16. nodular vasculitis, 17. spontaneous panniculitis of Rothmann-Makai, 18. metastatic neoplasm and lymphoma. The clinical picture as well as the report of biopsy will give the correct diagnosis.

There is no specific therapy for this disease. The sulfonamides have been reported to give good results. Neither penicillin nor aureomycin has had any effect. Shuman has reported a two months' remission with x-ray therapy; in his case there was no response to antimicrobial agents, and cortisone therapy succeeded in producing a normal temperature for 5 days. Cortisone and ACTH brought about marked remission as reported by Drew et al.[6]

Symptomatic and supportive therapy seems best for the patient, although recently salicylates and rather heavy doses of antihistamines have been reported with equivocal results. Arnold[1] has reported good results from intermittent treatment with sulfapyridine. Friedenberg administered cortisone to one of his patients but had to discontinue it because the biopsy site broke down.

CASE REPORT*

A 57-year-old white female came to the clinic on February 19, 1953. Her presenting complaints were painful lumps or nodules which had been recurring for the past eight years. While she had never had any known fever when these nodes appeared, there was associated pain in the groins, also leg ache, backache, and at times nausea. If she remained on her feet very much, there was swelling of the feet.

She believed the nodules were recurring more frequently. When the nodules disappeared, a sunken area would remain. When the nodules first appeared, in 1945, they recurred at varying intervals; during the past year they had been following one another almost continuously, and she was almost completely disabled. It was her impression that trauma was the inciting factor.

Family history revealed that her father died at the age of 86 of cancer of the prostate. A paternal aunt had diabetes. She had had the usual childhood diseases with a history of typhoid fever and questionable rheumatic fever. She was married, with three living children. She had had a hysterectomy at the age of 47.

Physical examination revealed a rather obese white female of stated age. The blood pressure was 116/65, pulse 86 and the temperature 99° on admission, which was the highest during this observation. On the lateral surface of the left thigh was an indurated area about 5 cm. in diameter, which was tender and reddened. This seemed to be attached to the skin. Scattered over the lower extremities were dimpled areas which the patient stated were sites of former lesions.

Laboratory reports revealed the hemoglobin to be 82 per cent or 14 gm., red blood cells 4,250,000, white blood count 7,950, with 2 eosinophiles, 2 stabs, 38 segments, 55 lymphocytes, and 3 monocytes in the differential. The Kline was negative. The nonprotein nitrogen was 29 mg. per cent, creatinine 1.67 mg. per cent and urea nitrogen 12.5 mg. per cent. The sedimentation rate was 11 mm. per hour, by the Westergren method. The urine was negative for albumin and sugar, with a specific gravity of 1.016. Skin tests for histoplasmosis and coccidioidosis and the first and second tuberculin tests were negative. The chest x-ray was considered negative.

Biopsy on February 21, 1953, revealed tissue from the left thigh weighing 55 grams and consisting of skin of elliptical form measuring 6 x 3 cm., with a 3.5 cm. thick fat tissue attached. Multiple sections showed fat tissue arranged in lobules. Beneath the surface was a firm area, band-like, with the appearance of fat tissue with whitish, smaller nodules. This hard area, extending throughout the specimen, was 8 mm. thick. Microscopic findings showed the epidermis well preserved with normal structure. The corium showed collagenous fibers and groups of sweat glands; there were several blood vessels surrounded with lymphocytes, especially monocytes. The lesion was situated in the subcutaneous fat tissue and consisted of cellular accumulations of histiocytes. There were many small spaces which were surrounded with macrophages and giant cells. Many large cells with foamy cytoplasm were noted. There was no evidence of neoplastic growth. The pathological diagnosis was nonsuppurative panniculitis (Weber-Christian disease).

The patient recently reported she had had two mild episodes shortly after hospitalization. For about 5 months she had no recurrence, but in the latter part of September, 1953, a new area appeared with typical manifestations.

* The patient was referred by L. G. Heins, M.D., Abilene, Kansas.

HISTOLOGY

The microscopic changes in Weber-Christian disease are so similar to those seen in localized lipogranuloma of traumatic origin that neither lesion can be differentiated on histological grounds alone. In the earliest stage, lipogranuloma consists of alteration of fat cells in the subcutaneous tissue. By disruption of the cell membranes, fat droplets are liberated from the fat cells and form globules of considerable size. These globules become surrounded by macrophages and by giant cells of the foreign body type. Macrophages, distended with fat droplets, are seen throughout the affected tissue. They transport the fat debris into perivascular and perineural lymphatic vessels, and some reach regional lymph nodes. The swelling of the regional lymph nodes may lead to a wrong clinical diagnosis of Hodgkin's disease or cancer with metastases. Focal lymphocytic infiltration is usually present, but polymorphonuclear leucocytes, plasma cells, and eosinophilic cells are either rare or absent. Globules of masses of free fat finally become entrapped by fibroblasts, which form connective tissue and later become rather dense hyaline scar tissue.

ETIOLOGY

Lecene and Moulonguet[11] believe that the primary and basic factor preceding lipogranuloma is the transformation of neutral fat into irritating fatty acids and soaps by lipase. Lipase, according to these authors, can be liberated from blood following traumatic hemorrhage or can be carried to the injured area by the blood stream. Since blood pigment is usually absent in the lesions of Weber-Christian disease, and since autopsy studies have revealed, in addition to the subcutaneous lesions, the same changes in epicardial, peripancreatic, periadrenal, peri-anal, and mesenteric fat tissue, we must assume that in Weber-Christian disease the etiological agent is blood-borne and acts on the traumatized fat cells of the subcutaneous tissue.

The lipase content of the blood is dependent on the function of the pancreas. In contrast to the normal levels of serum amylase, in chronic disease of the pancreas serum lipase is increased in about one-half of the cases of carcinoma of the pancreas, in more than one-half of the cases of carcinoma of the papilla of Vater, in 10 to 15 per cent of the cases of gallbladder disease, occasionally in duodenal ulcer, hepatitis, liver cirrhosis, chronic pancreatitis, and pancreatic obstruction. In conditions not primarily involving the pancreas, increase in serum lipase has also been observed, indicating a secondary pancreatic involvement.

There is a single histological description of the pancreas in the literature on cases of Weber-Christian disease. Mostofi and Engleman found, in their fatal case of Weber-Christian disease, that the acinar epithelium of the pancreas had a pale vacuolated cytoplasm suggesting fatty or hydropic degeneration. We therefore propose, as a working hypothesis, an increase in serum lipase as one of the underlying causes of Weber-Christian disease. The released and activated lipase acts secondarily on traumatized fat tissue.

Our patient associated trauma with her disease. This has been reported by other authors.[2, 7] It is conceivable that on many occasions the trauma may be so slight as not to be remembered by the patient.

Bendel[3] has suggested that a noxious stimulus produces a metamorphosis of the subcutaneous fat. This in turn acts as a foreign body, producing a foreign body response, with the reticuloendothelial system playing a large part of the syndrome. It is thought that, if this were true, the trauma may so change

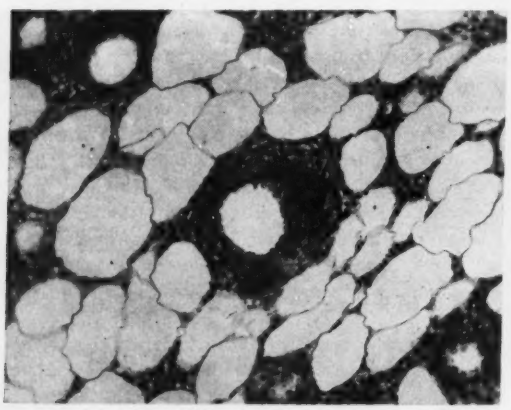

Figure 1. Early stage of lipogranulomatous lesion. In the center a ring of histiocytes and one giant cell surround a cystic space filled with altered fat.

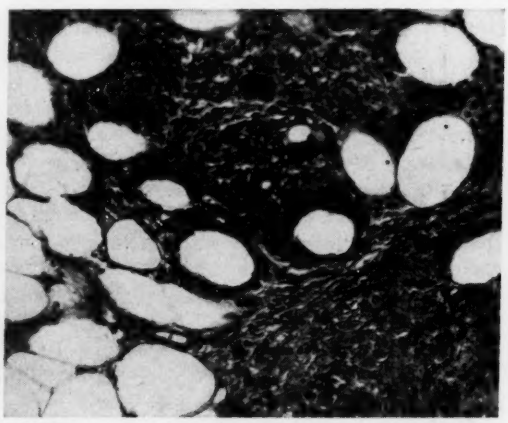

Figure 2. Later stage. Dense accumulation of lymphocytes and histiocytes with 2 giant cells. Fibroblasts have formed collagenous fibers.

the structure of the fat molecule as to bring about this response.

Allergic reasons have been suggested as causing the response.[3, 4, 6] Brudno[4] regarded the syndrome as an allergic systemic reaction to nonspecific stimuli with focal manifestations. He advances the theory that this is an antigen-antibody reaction. In our case no definite history of allergy could be determined.

CONCLUSIONS

Another case of Weber-Christian disease in which trauma is considered as an inciting factor is reported. In this case no history of febrile reaction could be obtained.

Elevation of serum lipase plus trauma may be the underlying cause of this disease.

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Addison's Disease Complicated by Pregnancy: A Case With Postpartum Hypertension

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Pregnancy is a serious complication for the patient with Addison's disease, for it may precipitate acute adrenal cortical insufficiency. The first review of cases of Addison's disease with pregnancy reported a maternal mortality rate of approximately 50 per cent.[1] By 1950, accumulated case reports indicated that maternal mortality had progressively diminished by virtue of improved management of adrenal crisis. Since the use of cortisone, uneventful pregnancy despite Addison's disease has been reported,[2, 3] but available cases are too few for statistical analysis. It would appear, however, that effective management of pregnancy in Addison's disease depends upon anticipation of adrenal crisis and upon recognition of other potential complications which may occur during the pregnancy.

Adrenal crisis may initially appear during the first trimester of pregnancy, when hyperemesis, with electrolyte, water, and carbohydrate loss, is a precipitating factor. During the second and third trimesters, adrenal crisis is uncommon. Instead, desoxycorticosterone acetate overdosage may cause maternal death, as hormonal requirements are lowered by the sodium retaining effect of progesterone and the possible elaboration of adrenocortical-like substances by the placenta. Fetal adrenal secretion is probably insufficient to affect maternal electrolytes.[4] Maternal mortality in Addison's disease is threatened most frequently during delivery and puerperium, when hemorrhage, trauma, and withdrawal of the placental progesterone may precipitate adrenal crisis. The fetal mortality rate is insignificant among term pregnancies, and spontaneous abortion is uncommon. Therapeutic abortion is hazardous.

Postpartum hypertension is an event not usually anticipated as a complication in Addison's disease. In the case following, cortisone and desoxycorticosterone acetate were used in treatment, and the principal complication was hypertension occurring on the fifth and sixth postpartum days.

CASE REPORT

A white woman, age 20, gravida 1, para 0, was first seen during pregnancy at the Wichita Clinic

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on June 30, 1952, when she complained of nausea. The estimated date of confinement was February 9, 1953.

Past history revealed that in 1951 a dermatologist had recognized Addisonian pigmentation of one year's duration, and she visited the Mayo Clinic* soon afterwards, where the diagnosis was confirmed. Treatment had consisted of 5 mgm. of cortisone twice a day, 2 mgm. of desoxycorticosterone acetate twice a day buccally, and 3 gm. of supplementary salt daily. The blood pressure had been 96 to 106 mm. Hg. systolic, and 64 to 78 mm. Hg. diastolic.

Physical examination and routine laboratory examinations were normal, except for pigmentation of the lip and a generalized darkening of the skin. The weight was 127 pounds and the blood pressure 90/60. The blood chemistry determinations during and following the pregnancy are indicated in Table I.

TABLE NO. I
BLOOD DETERMINATIONS

Date	*Sodium Meq/L*	*Potassium Meq/L*	*Chlorides Meq/L*	*CO_2 Meq/L*	*Sugar Mgm. %*	*Urea Nitrogen Mgm. %*
July 3	139	3.95	100			
Sept. 3	142	4.55				
Jan. 8	147.5	5.00				
Jan. 16	137	5.40	106	10.6	80	
Jan. 17			104	12.8	81	11.2
Jan. 19	140		106	13.9		
Jan. 21	135.5	4.20	96	16.9		
Jan. 22	133	5.10	98	18.2		

During the first trimester, no hyperemesis occurred. Treatment included 10 to 25 mgm. of cortisone in divided daily doses, 2 mgm. of desoxycorticosterone acetate twice a day buccally, and 3 gm. supplementary salt daily. At three and one-half months' gestation, dependent edema appeared. Salt tablets and desoxycorticosterone acetate were voluntarily discontinued for three weeks, after which the blood pressure was 82/44 mm. Hg.

During the second and third trimesters, while the aforementioned treatment was continued, the blood pressure was 96 to 100 mm. Hg. systolic and 60 to 70 mm. Hg. diastolic. Several infections of the respiratory tract were tolerated without incident. Urinalysis throughout the course of pregnancy showed no albuminuria or abnormal cellular elements. No edema was present except for a slight amount for a few days each the 5th and 7th months of gestation.

On January 15, 1953, at 5:00 p. m. the patient was hospitalized, having had uterine contractions for 12 hours. Examination revealed slight vaginal bleeding; the cervical os was firm, uneffaced, and without dilatation. Fetal heart sounds became more distant because of increased uterine tonicity. A normal fetus was delivered at 1:35 a. m. on January 16 by cesarean section. A diagnosis of abruptio placentae was confirmed by inspection of the uterus and placenta.

On January 15, before hospitalization, the patient had taken 10 mgm. of cortisone orally. At 5:00 p. m., on January 15, she received 100 mgm. of cortisone intramuscularly and 25 mgm. orally, and the blood pressure was 104/70 mm. Hg. At 10:30 p. m., 25 mgm. of cortisone was given orally, and at 12:45 a. m., on January 16, 100 mgm. of cortisone was given intramuscularly prior to surgery. During surgery she received methoxamine hydrochloride (Vasoxyl R), and the maximum blood pressure was 140/90 mm. Hg.

At 8:00 a. m. on January 16, 50 mgm. of cortisone was given intramuscularly, and an injection of 1,000 cc. of 10 per cent glucose in physiologic saline was begun. This was the only occasion on which intravenous solution was given. Salt was added generously to the diet. On January 16, laboratory data was satisfactory except for indicating acidosis, for which 0.6 gm. of sodium bicarbonate three times a day was given. Unfortunately, the oral intake of water and salt was not measured, for the patient felt unusually well during the first five days postpartum. Urinary output and 24-hour urine chloride excretion were determined (Table II). Treatment and blood pressure levels are indicated in Figure I. The regular dose of 2 mgm. of desoxycorticosterone acetate two times a day was given on three of the first five postpartum days.

TABLE NO. II
URINE EXCRETION

Date	*24 Hour urine Volume in cc.*	*24 Hour Chlorides (Total meq.)*
Jan. 17	2200	66
Jan. 18	2600	143
Jan. 19	2600	98
Jan. 20	2300	161
Jan. 21	3000	240
Jan. 22	2500	225
Jan. 23	1900	238
Jan. 24	1700	187
Jan. 25	2500	225

On January 21 at 2:00 a. m., the fifth postpartum day, she complained of headache. The blood pressure was 170/100 mm. Hg. Physical examination showed no edema. Serum electrolyte determinations were satisfactory, and less acidosis was present. This incident occurred 40 hours after she received 50 mgm. of cortisone intramuscularly. Diuresis had occurred during the preceding days, reaching its peak on January 21.

On January 21, the dose of desoxycorticosterone acetate was decreased to 2 mgm. daily for the next

* This case is being included as one of a series by Dr. William M. McConahey and Dr. A. B. Hunt, Mayo Clinic, in another publication.

two days, and the administration of sodium bicarbonate was discontinued. The last injection of 50 mgm. of cortisone was given on January 21, while the regular dose of cortisone was continued.

On January 22, at 6:00 a. m. she again had a severe headache. The blood pressure was 190/100 mm. Hg., decreasing by 8:00 a. m. to 140/80 mm. Hg. without treatment. Thereafter, the blood pressure gradually decreased to the prenatal level, and the patient had no more headaches. She continued to receive the same treatment prescribed before pregnancy.

DISCUSSION

Although acute adrenal insufficiency is the most common severe complication of Addison's disease during late pregnancy and early puerperium, the development of a temporary hypertension has been reported several times. This hypertension has been either unexplained or attributed to overdosage of salt and DCA, or to late toxemia of pregnancy. Hypertension was attributed to overdosage of salt and DCA in separate cases reported by Brent,[5] Loeb,[6] and Richards.[7] Brent's case developed an elevation of blood pressure on the first postoperative day. Loeb had a case with hypertension during the final two months of pregnancy. Richards' case was treated with Eucortone, salt, and DCA, and had an elevation of blood pressure and edema after delivery requiring reduction of the DCA dose on the fourth postpartum day.

Cohen[8] reported a case of preeclamptic toxemia with edema, albuminuria, and a blood pressure of 188/128 during labor, with a normotensive state following postpartum diuresis. This was an unusual occurrence, since Brent found no reports of eclampsia among 40 cases which she reviewed.

Galloway[9] reported a case with acute adrenal insufficiency at 7 months gestation; an undesignated number of days postpartum, the blood pressure rose to 170/80. He attributed the hypertension to overactivity of the adrenal glands with the cessation of pregnancy.

One of the patients reported by Knowlton, Mudge, and Jailer[10] in 1949 had hypertension during the last month of pregnancy, but she was normotensive postpartum. In 1950, Jailer et al.[11] reported a case with a blood pressure of 160/100 on the sixth postpartum day.

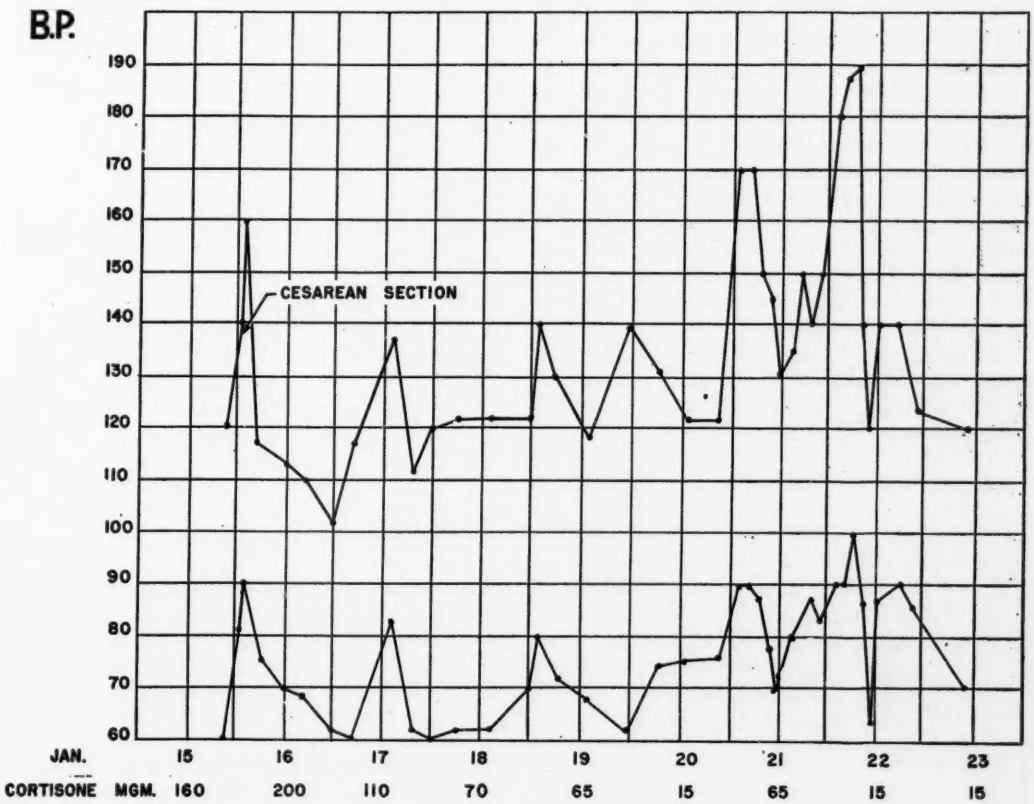

Figure I. The postpartum blood pressure and daily dosage of cortisone are shown.

In our case we lack evidence determining the cause of hypertension although several possible contributing factors may be considered. It is doubtful that the salt-retaining effect of the increased sex steroids during pregnancy[12, 13] was an important factor since the blood pressure was normal until after the time of delivery, there was a good urinary output during the entire early puerperium, and the patient's weight gain during the pregnancy was only 23 pounds. In the absence of edema and albuminuria, we believe toxemia was not present in this case.

There are several mechanisms by which cortisone might have influenced the blood pressure. Cortisone has been shown to increase the blood volume by shifting fluid from the intracellular to the extracellular[14] space. It also has the property of increasing blood pressure in Addison's disease or renal insufficiency,[16] in cases in which the weight gain and fluid retention are not considered sufficient to be the cause. Cortisone may have a vasoconstrictor effect since adrenalectomized patients will have a prompt rise in blood pressure when given cortisone with nor-epinephrine.[17] Also, cortisone decreases the hypotensive effect of tetraethylammonium chloride.[18]

However, we doubt that cortisone was the cause of the hypertension in our patient, since other cases mentioned in the literature had hypertension without large doses of cortisone; furthermore, the case reported by Wells and West received cortisone in an amount similar to ours without developing hypertension. Further information might have been obtained from our patient had we been able to repeat the same medication while she was not pregnant to establish whether hypertension might have been produced. The acidosis was thought to be due to the patient's Addison's disease, but renal insufficiency must be more thoroughly excluded.

We believe that there may be some as yet undetermined factor related to late pregnancy in the postpartum period in Addison's disease which predisposes to hypertension. More detailed studies of the electrolyte pattern and vascular responses during the postpartum period in Addison's disease seem to be indicated.

SUMMARY

1. A case of Addison's disease complicated by pregnancy, with survival of both the patient and baby, is reported.

2. The chief complication of postpartum hypertension is discussed.

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Have you ever rightly considered what the mere ability to read means? That it is the key which admits us to the whole world of thought and fancy and imagination? To the company of saint and sage, of the wisest and the wittiest at their wisest and wittiest moment? That it enables us to see with the keenest eyes, hear with the finest ears, and listen to the sweetest voices of all time? More than that, it annihilates time and space for us.—*James Russell Lowell.*

BLUE SHIELD

More About Enrollment

Plans for the 1954 Blue Cross-Blue Shield non-group community enrollment program were announced in the public press early this month, along with a list of the annual enrollment months for 99 of our counties. Activity is also going ahead for the continuous enrollment experiment which is to be conducted in Shawnee, Sedgwick, Osborne, and Barber counties.

While the opening dates for these four counties where there is to be continuous enrollment is still uncertain, campaign activities are already under way in many of the other counties, and some enrollments have already been held. In the new program, annual enrollment months have been established in every county included in the Kansas plan. Exact dates within each month may vary, but the month in which the non-group enrollment occurs will be the same every year. Enrollment months, except where there is continuous enrollment, are as follows:

January: Brown, Cheyenne, Coffey, Ellsworth, Nemaha, Osage, Rawlins, Rush, and Washington.

February: Cherokee, Cowley, Doniphan, Douglas, Lincoln, McPherson, Ottawa, Rooks, Saline, Sherman, Harvey, Miami, and Montgomery.

March: Bourbon, Ellis, Finney, Franklin, Jewell, Labette, Marion, Marshall, Pratt, Reno, Smith, and Thomas.

April: Chase, Chautauqua, Clay, Dickinson, Elk, Haskell, Gray, Jefferson, Lane, Linn, Seward, Meade, Morris, Republic, Rice, Russell, Scott, and Sumner.

May: Butler, Geary, Greeley, Hodgeman, Jackson, Lyon, Mitchell, Ness, Pawnee, Phillips, Stafford, Wallace, and Wichita.

June: Crawford, Greenwood, Harper, Kingman, Wilson, and Woodson.

September: Anderson, Barton, Graham, Riley, Sheridan, and Wabaunsee.

October: Allen, Clark, Comanche, Edwards, Ford, Kiowa, and Neosho.

November: Atchison, Cloud, Decatur, Grant, Hamilton, Kearny, Morton, Norton, Pottawatomie, Stanton, and Stevens.

December: Gove, Leavenworth, Logan, and Trego.

RETENTION IMPORTANT

It has already been pointed out that this new method of "regular" enrollment activity can be possible by the introduction of a new type of application which contains a fairly detailed and comprehensive statement of health. This new health statement-type of application card, however, will apply only to the *new* members (or applicants).

Here, again, the co-operation of Blue Shield participating physicians will be necessary in helping to remind all present members that they are not affected by this new program unless they drop their membership, and then seek to re-enroll. It cannot be emphasized too strongly to present members that they are still members in good standing, and that the valuable benefits of Blue Cross-Blue Shield are still theirs with no changes.

WAITING PERIODS

It has been necessary to establish a new group of conditions which are subject to an eight-month waiting period. They are as follows:

1. Obstetrical services.
2. Operations for the removal of tonsils and/or adenoids.
3. Treatment for tumors or growths.
4. Operations for hernia.
5. Operations for conditions of gall bladder, rectum, or genito-urinary tract.

While there may be some objection to this from the doctors, when one considers the alternative to establishing this clear-cut list of conditions, the latter course seems the best one to follow. Otherwise, it would be necessary to determine whether or not each case was for a condition which pre-existed the date of membership. This would involve considerable correspondence with doctors and a great deal of poor public relations and misunderstanding. On the other hand, the establishment of a clear-cut list on which there would be an eight-month waiting period will not involve all this administrative difficulty.

Blue Cross-Blue Shield will need the utmost in co-operation from the physicians and hospitals in Kansas. The underwriting of new memberships, the decision whether to refuse an applicant entirely or to accept him with a rider excluding treatment for certain conditions—these are situations in which the medical profession will be called upon to help the lay staff. No doubt it will be well worth some sacrifice of time and effort if it can result in a program of enrollment which can offer this coverage to every eligible person in Kansas.

The keystone of every public health endeavor must always be the private practitioner of medicine, who must rely on the local health department for assistance. If the health department is properly organized and carries out the objective for which it was designed, it will support and improve the private practice of medicine.—*Vlado A. Getting, M.D., J.A.M.A., Sept. 26, 1953.*

K.M.S. annual meeting, May 2-6, 1954, Topeka.

PRESIDENT'S PAGE

DEAR DOCTOR:

The 19th of February there will be an A.M.A. sponsored meeting in Denver on veterans' medical care. At this writing, it is the intent of your president to attend.

The thinking of the A.M.A. on veterans' medical care has always been in total accord with full and complete and continued medical care for service connected disabilities. But the A.M.A. has rigidly opposed medical care for non-service connected disabilities and the extension of the time of presumption of service connection to the point where it is becoming ridiculous.

It is certainly the duty of our government and us as taxpayers to give every veteran who was disabled by service connected injury or illness every consideration in the care of that disability, in order that he may return to a useful and happy life. But it is neither our duty nor our obligation on a national scale to take care of the medical needs of any veteran with an illness that has no service connection. This is pure socialization of medicine, and it has no place in the American way of living. It is just another wedge in the door that leads to the pathway to socialism.

Each and every one of us should give this matter our closest attention. We should aid the A.M.A. in its fight to curtail the further expansion of Veterans Administration hospital facilities and medical care for those conditions which should be procured from the facilities that exist in our local communities.

EDITORIAL COMMENT

Prehistoric Medicine

Skeletal and mummified remains of ancient man have afforded anthropologists a considerable, although by no means a uniform, opinion upon disease in prehistoric time. A pamphlet on this subject published by Ciba Pharmaceutical Products, Inc., some time ago was recently reviewed and appeared of sufficient interest to warrant a résumé at this time.

Arthritis and spondylitis appear among all people regardless of climate, diet, life habits, or period of time. A Neanderthal skeleton of about 40,000 B.C. is an example, and in the neolithic period some 30,000 years later numerous remains attest to the presence of vertebral ankylosis and atrophied intervertebral discs. The cave man from the Old Stone Age in Europe suffered from arthritis deformans, and the cave bears he fought had it also. One scientist reports that 40 per cent of the Egyptian skeletons showed spondylitis. In addition, many had arthritis of knee and shoulder joints as well as ankylosis of the pelvis.

Tuberculosis also seems to be identifiable in the remains of ancient man, although this condition is not so prevalent. It appears sporadically in skeletons from antiquity but is notably absent as, for example, in the 6,000 skeletons from Nubia dating about 3,500 B.C. Tuberculosis appears earlier in Europe than in Egypt. One Bronze Age tuberculous spine was found in France, and many evidences were obtained from the Aztec and Inca Indians.

Rickets appeared in early man, but its incidence was apparently not high. Some authorities insist evidences of this condition may be located as far back as the Cro-Magnon man. Rickets appear to have been more frequent among the Indians in this hemisphere than among European aborigines.

Numerous cranial deformities have been noted in the remains of ancient skeletons from all periods. Various authorities of presumed integrity have claimed to have identified "button osteomata" and leontiasis ossea in Chinese prehistoric crania.

Fractures were of course common in prehistoric man. An interesting feature is that forearm fractures in females among French neolithic skeletons are so frequent that they appear to be the rule rather than the exception. Head injuries were the most common of all traumatic lesions, probably inflicted through warfare and as the quickest method of ceremonial killing. Some authorities hold that the latter appears common enough to have been in wide practice. Evidence of healed injuries to the head are plentiful, and long before the era of written history trepanning became common in medical practice.

Prehistoric syphilis has been identified through skeletal diagnosis from many areas of the world, but principally in prehistoric Peru, Mexico, and North America. The criteria are found in cranial lenticular exostoses or lesions, premature closure of vault sutures, sabre-tibia and tibial hyperostosis, ogival form of the palate, and dental malformations, as erosion, impaction, microdontism, hypercementosis, bifid roots, Carabelli's cusp, and hypoplastic enamel.

A dissertation upon prehistoric man's knowledge of anatomy, pathology, and medicine becomes theoretical. It can be argued, however, that man's observations and instincts afforded him greater knowledge even in antiquity than may presently be realized. For example, certain primitive people today possess knowledge of anatomy and surgery that is amazing, and from the evidence of healed fractures it appears that some form of medical care must have been given. It must further be presumed that injuries to the skeletal structure must frequently have caused deep wounds which certainly would have required some form of closure. There is also evidence from early pictorial records that ancients in some parts of the world performed cesarean sections.

No knowledge is available as to when splints were first applied to fractures or when casts were used. It is, however, not unreasonable that the easing of pain through an immobilized limb would readily be recognized and repeated under similar circumstances. There are sufficient amputations to indicate that this also was frequently resorted to, possibly following a mangling injury or a poisonous bite.

The earliest known surgical treatise exists on papyrus from the 18th dynasty of Egypt. This describes the case history of 48 instances of trauma. In this work Egyptian surgery was at least advanced to the point where hemorrhage was arrested by pressure, where foreign bodies were extracted, where minor amputations were performed, wounds closed, dislocations reduced, abscesses cauterized, cysts incised and drained, and fatty tumors removed. In the treatment of wounds there was exploration, cleansing, and suturing or plastering of the wound edges. Described in this document were enemas, gargles, ear drops, and medicated pledgets in body cavities. There was no antisepsis, but there were ideas of fumigation. Obstetrics was in the hands of midwives, but there were specialists for the eye and for the belly. Descriptions of diseases from this period indicate the presence of "renal and vesicular calculi, arteriosclerosis, anthracosis, pneumonia which had progressed to hepatization, appendicitis, cirrhosis of the liver, splenic hypertrophy, genital prolapse, vesico-vaginal fistula . . ." and others including smallpox.

The physician of that period was versed in detail

concerning the evidences of certain conditions, the course of the disease, and the prognosis. It was recommended that upon seeing the patient he pronounce one of three verdicts: the first, "an ailment I can treat"; the second, "an ailment I will contend with"; and third, "an ailment not to be treated." The author of this article reminds his readers that this is faith, hope, failure.

Events in Washington

Events in Washington are transpiring with such rapidity that the lapse of time between the preparation of material and its appearance in the JOURNAL may render mention of the information obsolete. This, then, is historic as of the close of January, 1954.

The President has sent numerous messages to the Congress and has frequently mentioned items of interest to medicine. The following excerpts come from President Eisenhower's State of the Union message:

Socialization of Medicine: "I am flatly opposed to the socialization of medicine. The great need . . . can best be met by the initiative of private plans. But it is unfortunately a fact that medical costs are rising and already impose severe hardships on many families. The federal government can do many things and still avoid the socialization of medicine."

Research: "The federal government should encourage medical research in its battle with such diseases as cancer and heart ailments, and should continue to help states in health and rehabilitation."

Hill-Burton Program: "The present . . . act should be broadened to assist in the development of adequate facilities for the chronically ill . . . of diagnostic centers, rehabilitation facilities and nursing homes."

Reinsurance of Health Plans: "The war on disease . . . needs a better working relationship between government and private initiative. . . . A limited government reinsurance service would permit the private and non-profit insurance companies to offer broader protection to more of the many families which want and should have it."

Rehabilitation: "The program for rehabilitation of the disabled especially needs strengthening. . . .This program presently returns each year some 60,000 handicapped individuals to productive work. Far more disabled people can be saved each year . . . if this program is gradually increased."

Military Dependents: "Pay alone will not retain in the career service . . . the necessary numbers of long-term personnel. I strongly urge, therefore, a more generous use of other benefits important to service morale. Among these are more adequate living quarters, and medical care for dependents."

Medical Tax Deductions: " . . . we propose more liberal tax treatment for dependent children who work, for widows or widowers with dependent children, and for medical expenses."

Veterans: "The internal reorganization of the Veterans Administration is proceeding with my full approval. When completed, it will afford a single agency whose services, including medical facilities, will be better adapted to the needs of those 20 million veterans to whom the Nation owes so much." (There was no further reference to VA in the address.)

Social Security: "I ask that this extension (to 10,000,000 more persons) soon be accomplished. This and other major improvements . . . will bring substantial benefit increases and broaden the membership of the insurance system, thus diminishing the need for Federal grants-in-aid. . . ."

Since that time the President has spoken more completely upon the subject of Federal Health Service Reinsurance and on loans to non-profit health associations. He has further urged mandatory coverage for doctors and other self-employed and professional people under social security. These issues have not yet been clarified through the introduction of legislation so should perhaps not be discussed until details are more completely available.

Doctors at War and at Home

The total number of American service men wounded in World War II was about 700,000, of which the Army accounts for nearly 85 per cent. This figure is about three times as high as the first war.

American doctors drew high praise for their work since the fatality rate among those wounded was the the lowest in history for any army in the world. The fatality rate in the Army was 4.4 per cent, which is slightly more than half of the 8.3 per cent in the Army during World War I. Even a greater contrast was evidenced in the Navy and Marines where, in World War I, 12 per cent of those wounded died, as compared to 2.9 per cent in the second war. Figures available from the Korean fighting show the fatality rate among our wounded as 2 per cent, which of course is less than half percentagewise of the record breaking 4.4 per cent of World War II.

Much of this success is attributed to the use of sulfa drugs on a wide scale and the speeding up and development of penicillin. Use of blood and blood derivatives played an important role, as did effective methods of treating shock due to blood loss.

Many medical problems were met in World War II. One important factor was the problem of malaria control, when our major source of supply of quinine

was cut off by Japanese conquest of the East Indies. This problem was overcome by the spraying of disease-bearing mosquito breeding places and the use of new anti-malaria drugs which were developed and manufactured on a large scale.

Control of venereal disease, the vaccine for yellow fever, and the use of DDT were also aiding factors in the second war.

Much can also be said for the doctor population who remained at home to care for our civilian population. Doctors, overburdened with work, used resources so efficiently that instead of an expected increase in civilian mortality the opposite was quite apparent. During the years 1941 through 1945, the death rate in our country declined about 15 per cent, as compared to the preceding five-year period.

Where statistics are available in European countries, the opposite was true. The death rate among the civilian population in France showed an increase of 30 per cent in one year, the Netherlands 75 per cent, Belgium 20 per cent.

In summation, we find that while the doctors in service were instrumental in establishing new records in World War II, by cutting in half the fatality rate among the wounded, the civilian doctors held their own by aiding in the decrease of civilian mortality by over 15 per cent, as compared to the pre-war period.

Memorial Fund

The Woman's Auxiliary to the Kansas Medical Society has recently created a memorial fund which represents a departure from previous custom and a subject that well might occupy the attention of the medical society. The Auxiliary currently recommends that instead of bestowing flowers to the memory of deceased esteemed members, the Auxiliary will accept contributions to a nurse scholarship fund.

It is anticipated this will be used in the form of a loan that will be repayable according to terms defined by a special committee already appointed, and that interest on this loan will be low and possibly will begin after the student has completed her education. The present committee consists of Mrs. William Brewer, Hays; Mrs. Richard O'Donnell, Ellsworth, and Mrs. William T. Braun, Pittsburg.

Contributions to this special memorial fund may be given by any friend in the name of any Auxiliary member. Loans will be made through this fund by the committee according to applicants for loans and recommendations from the various schools of nursing in Kansas. In the beginning this must be used cautiously because the amount is small, but as this memorial fund increases in size it is hoped that many student nurses may benefit therefrom.

It is mentioned here as a worthwhile project on the part of the Auxiliary and because this represents an effort to which numerous doctors may wish at different times to contribute.

Vaccinia Immune Gamma Globulin

The Kansas State Board of Health calls attention to an attempt to gauge the effectiveness of a specially prepared vaccinia immune gamma globulin. This gamma globulin, manufactured by the Department of Pediatrics at the University of California Medical Center, is to be used in the prevention and therapy of serious complications of smallpox vaccination. Any physician who sees such complications is urged to contact the researchers immediately so that a supply of the material can be made available.

The complications, in the main, are generalized vaccinia, eczema vaccinatum, and progressive vaccinia (failure to produce specific antibodies) or vaccinia necrosum. Most patients so affected will be seen by physicians in clinical practice, in contagion hospitals, in teaching centers, public health departments, and well baby clinics.

Vaccinia immune gamma globulin is a solution of the globulin component of human blood collected from volunteer donors of the armed services who have been successfully vaccinated against smallpox from four to eight weeks prior to this blood donation. It was found that their neutralizing antibody titers were maximal at that time. The material was tested in India for the specific prevention of smallpox in exposed susceptible family contacts, and experience indicates that it is successful.

It is the thought of the University of California physicians that vaccinia immune gamma globulin can be distributed to best advantage on a request basis; the supply is not large enough to allow national distribution for storage.

Between 20 and 60 per cent of the cases of complications of smallpox vaccination are fatal, despite intensive fluid and antibiotic therapy. Therefore, it is essential that physicians seeing such patients communicate with the researchers by telephone or telegram so that the material may be dispatched by air express, free of charge. The address to be used is C. Henry Kempe, M.D., Department of Pediatrics, University of California Hospital, San Francisco 22, California, MOntrose 4-3600, Extension 371. The university hospital will refer night calls to laboratory personnel.

Make hotel reservations now for the annual meeting, May 2-6, 1954, Topeka.

ACTIVITIES OF MEMBERS

Dr. James P. Haigler, Hays, announces that Dr. Rex C. Belisle is now associated with him in general practice. Dr. Belisle, a graduate of the University of Kansas School of Medicine, practiced for a short while in Plainville before beginning a three-year tour of duty with the Navy.

Dr. Winstan L. Anderson, Atchison, has been appointed to a two-year term as a member of a new city-county health board. He will represent the city. Dr. Edwin T. Wulff, representing the county, has been appointed to a three-year term on the same board.

Dr. Lee Rook, Kansas City, took office last month as president of the Wyandotte Academy of General Practice. Other officers are: Dr. M. R. Fitzpatrick, vice-president; Dr. Harvey L. Lloyd, secretary; Dr. A. W. Bradford, treasurer. Members of the board of directors are Doctors Emmerich Schulte, Frank J. Strick, and Gaylord P. Neighbor.

Dr. John B. Dixon, Parsons, was licensed as a private pilot last month.

Dr. Paul H. Wedin, Wichita, was speaker at a recent meeting of the Dickinson County Medical Society. His subject was "Surgical Disease of the Chest."

Dr. Lynn C. Hartman, director of the Cowley County Joint Board of Health during the past three years, resigned that position last month to devote her time to her home and family. Dr. Roscoe F. Morton is serving as health director pending appointment of a permanent director.

Dr. Warren F. Bernstorf, Winfield, took part in a panel discussion on "Ministry to the Sick," during the Kansas Christian Ministers' Institute held at Winfield early in January.

Dr. John L. Fatland, Council Grove, spoke before the Rotary Club in that city last month on the subject of "Trends in Medical Care."

Dr. Joseph E. Gootee was recently elected president of the Topeka Blood Bank for the year 1954, and Dr. G. F. Helwig was named secretary. Serving on the board of directors are Doctors John W. Cavanaugh, John L. Lattimore, Howard U. Kennedy, and David E. Gray.

Dr. D. M. Diefendorf, Waterville, has been named health officer of Marshall County. He replaces the late Dr. R. L. McAllister.

Dr. A. K. Ratzlaff, Goessel, was speaker at a meeting of the Fourth District Nurses' Association at Halstead last month.

Dr. O. R. Cram, Larned, and Dr. Mary Glassen, Phillipsburg, were recently elected directors of the Kansas Association for Mental Health.

Dr. William C. Menninger, Topeka, addressed the 53rd annual meeting of the Family Consultation Service in Wichita on January 28.

Dr. L. Lafe Bresette, Kansas City, has been named medical division chairman of the United Hospitals Building Fund in that city.

The Arkansas City Medical and Surgical Clinic has announced the dissolution of its partnership, effective February 28. The five physicians in the partnership are Dr. W. G. Weston, Dr. E. R. Maier, Dr. J. V. Sharp, Dr. R. F. Morton, and Dr. James E. Hill.

Dr. S. N. Chaffee, 85, Solomon, who has been in practice more than 50 years, retired from active practice on January 30. A feature story about him and his practice was published by the *Solomon Valley Tribune*.

Dr. Thomas L. Foster, Halstead, directed a program on mental health for the January meeting of the Halstead Parent-Teacher Association.

Dr. LeGrand Byington, Kansas City, has been elected chairman of the health division of the Social Planning Council of Wyandotte County.

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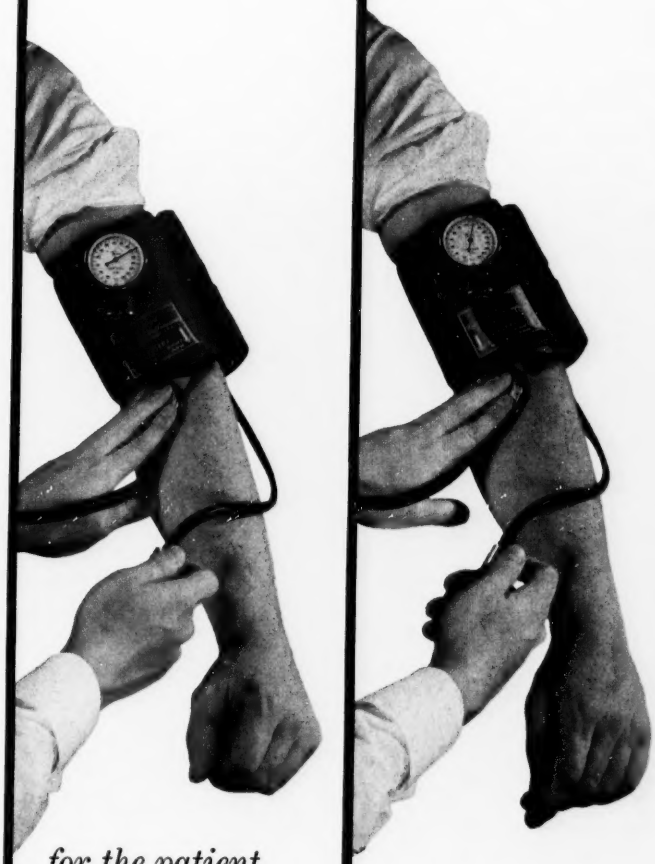

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1. Hafkenschiel, J. H., and Lindauer, M. A.: Circulation 7: 52, 1953.
2. Schroeder, H. A.: Circulation 5: 28, 1952.
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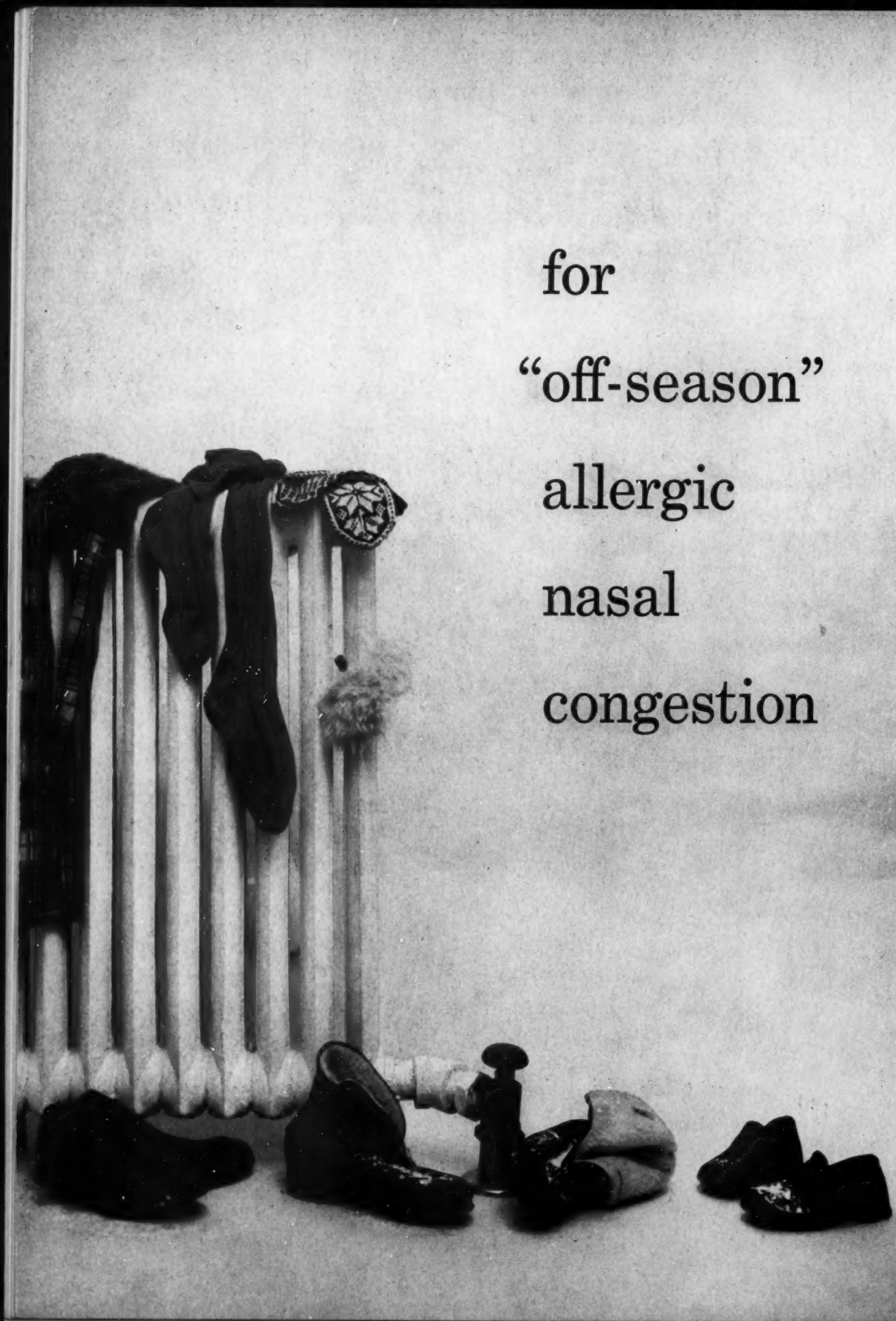
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1. Dill, J. L.: Postgrad. Med. 4:413, 1948.

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1. Hild, A. M.: Schweiz. med. Wchnschr. 71:557, 1941.
2. New and Nonofficial Remedies, J. B. Lippincott Co., Philadelphia, 1953, p. 200.

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COUNTY SOCIETIES

New officers of the Wyandotte County Medical Society, as reported last month, were installed at a dinner meeting held at the Town House Hotel, Kansas City, on January 9. Dr. Glenn R. Peters, retiring president, spoke on "Medicine, 1953," and Dr. J. Warren Manley, new president, discussed "Medicine, 1954." The doctors' wives were guests for the occasion, which was concluded with a dance.

A meeting of the Sedgwick County Society was held at the Lassen Hotel, Wichita, on January 5. Speaker of the evening was Dr. H. A. Schroeder, assistant professor of medicine, Washington University School of Medicine, who discussed "Medical Treatment of Hypertension."

Officers of the Franklin County Society for 1954 were elected at a meeting held at the Ottawa hospital on December 21. Dr. C. W. Henning was elected president; Dr. Louis N. Speer, vice-president, and Dr. James E. Wallen, secretary-treasurer.

A meeting of the Shawnee County Society was held in Topeka, January 4. The speaker was Mr. Doyle Howard, Kansas City, who explained the apparatus, equipment, and methods of administration of oxygen and other gases in therapy.

Members of the Saline County Society were hosts to the Golden Belt Medical Society at a meeting held at the Salina Country Club on January 14. Two Topeka physicians presented the scientific program, Dr. Clyde B. Trees speaking on "Intramedullary Pinning" and Dr. R. M. Brooker discussing "Differential Diagnosis of Surgical Diseases of the Lungs." A dinner and social hour followed the program.

Ground breaking ceremonies were conducted in Wichita last month at the site of the new $90,000 building of the Sedgwick County Medical Society. The ground, at Zimmerly and Hillside, was leased from the Sisters of St. Joseph.

The building, of brick and concrete, will provide auditorium space, executive offices, library, reading room, and quarters for the Medical Service Bureau. It will have approximately 5,400 square feet of floor space on one floor, and there will be off street parking for 200 cars.

Dr. Max W. Wells, Winfield, was elected president of the Cowley County Society at a meeting held at Christmas time at the Winfield Country Club. Dr. Newton C. Smith, Arkansas City, was chosen to serve as vice-president; Dr. R. B. White, secretary, and Dr. W. G. Weston as a new member of the board of censors. A dinner and program, shared with members of the Auxiliary, preceded the business session.

A meeting of the Wyandotte County Society was held at the City-County Health Building, Kansas City, on January 19. Mr. Joe Cohen, an attorney, spoke on "The Doctor in the Courtroom."

A series of health programs is being presented over the air on station KMAN, Manhattan, under the sponsorship of the Riley County Society. The programs have been produced by the American Medical Association.

Dr. J. T. Naramore, Larned, was elected president of the Pawnee County Society at a meeting held on January 14. Dr. T. D. Ewing, Bushton, was named vice-president, and Dr. S. T. Coughlin, Larned, was chosen secretary-treasurer. Dr. LeRoy Shepard, Larned, will be the delegate to the state meeting.

A Blue Cross-Blue Shield membership drive in Coffey County last month was sponsored by the Coffey County Medical Society.

Kansas Licenses to 48

Forty-eight physicians were licensed to practice medicine in Kansas last month, according to Dr. O. W. Davidson, secretary of the Kansas State Board of Medical Registration and Examination. Thirty-nine were licensed by endorsement, and the others successfully completed examinations given by the board in Topeka in December.

Those licensed by reciprocity and the cities in which they indicated they plan to practice are as follows: Berneil Walter Andrews, no location listed; Charles Edward Andrews, Kansas City; Eustace Vernon Ashley, Bushton; James Arnold Bertone, Topeka; John Edmund Birdsell, Topeka; Samuel Beach Chapman, Jr., no location listed; Rudolph Chess, Topeka; Marion O. Christensen, Kiowa; Charles DeHaan, Jr., Pretty Prairie; James Louis Diacon, Wellington; John Lewis Fatland, Council Grove.

Martin James Fitzpatrick, Kansas City; Wayne

Lewis Fowler, Concordia; Evan Lloyd Frederickson, Kansas City; Evalyn Stolaroff Gendel, Topeka; Jack Arnold Haley, Hanover; Edward Albert Heffner, Jr., Hutchinson; John Henry Hege, Lawrence; Lyle Travers Hooker, Osawatomie; Rupert Mitchell Jastram, Hutchinson; Margaret Elizabeth Joyce, Wichita; Lee Franklin Kramer, Cherryvale.

Burritt Samuel Lacy, Jr., Topeka; James Leon McGovern, Wellington; Anthony Wayne Miles, Wichita; John Francis Montague, Topeka; D. Harlan Morgan, no location listed; Van Sam Parmley, Wichita; Edward Bales Price, Jr., Kansas City; Mary Elizabeth Pucci, Manhattan; Norman Keith Pullman, Wichita; William Farthing Sargent, Topeka; Patricia Turk Schloesser, Topeka; Sanford Simon, Kansas City; David Marion Stahl, Kansas City; John Easter Sweeney, Topeka; John William Walker, no location listed; Paul Shan Williamson, Osawatomie, and Karl Arden Youngstrom, Kansas City.

Those licensed by examination are as follows: Harold Altman, Kansas City, Missouri; James Edward Baker, Topeka; Philip G. Danufsky, Kansas City; Joseph Martin Green, Topeka; Lois H. Lohrentz, Kansas City; Richard Lynn Meadows, Topeka; Robert G. Menninger, Topeka; William F. Smith, Jr., Topeka, and Vernon Earl Wilson, Kansas City.

THE KANSAS PRESS LOOKS AT MEDICINE

Editor's Note. In this section the JOURNAL *reproduces editorials relating to medicine which have appeared in the lay press. An effort is made to include both favorable and unfavorable comments, and the Editorial Board in no instance assumes responsibility for the opinions expressed.*

Doctors Don't Run to Washington

A short time ago a *St. Louis Globe-Democrat* reporter interviewed the president of the American Medical Education Foundation, and wrote a strong constructive story about that institution's work. Later, the paper ran an editorial in which it commended American medicine for the prodigious job it is doing in the field of medical education. It also praised the doctors for carrying out the job themselves instead of running to Washington for money.

Many people have been misled into the belief that the medical fraternity is perfectly satisfied with the status quo and is doing little or nothing to improve matters. That idea is 100 per cent wrong. Medical education is an excellent example. Our medical schools are operating under a heavy financial strain. The Foundation was founded in 1950 to do something positive to help. It has raised $2,700,000 from doctors alone. And, along with the National Fund for Medical Education with which it cooperates, contributions totaling $5,100,000 have been obtained during the last three years.

In every phase of medicine, hard work is quietly going on, and it has but one objective—to give the American people better and more extensive medical care. We see this in the endless research to learn more about the cause and cure and prevention of disease. And we see it as well in the search for sound ways and means to lessen the financial shock of illness.

It is true that medicine opposes dictation by government, even as it opposes tax subsidization of activities that are the responsibility of private groups and individuals. That opposition is based on the sure knowledge that the greatest progress for all will come by maintaining medicine in an atmosphere of freedom—not in an atmosphere of political coercion. —*Atwood Citizen-Patriot, January 14, 1954.*

DEATH NOTICES

EDWARD JACOB HAERLE, M.D.

Dr. E. J. Haerle, 65, who had practiced in Minneapolis more than 20 years and who had been Ottawa County health officer for 15 years, died at his home on December 29. A graduate of Southwest School of Medicine and Hospital, Kansas City, in 1912, Dr. Haerle first practiced in Niles. During World War I, he served in the Army medical corps for 14 months. He was an active member of the Saline County Medical Society. Among the survivors is his brother, Dr. Henry H. Haerle, Marysville.

CHARLES MOSES SIEVER, M.D.

Dr. C. M. Siever, 79, an honorary member of the Shawnee County Society, died at his home in Topeka on January 15. He received his medical degree from Dallas Medical College in 1903 and practiced consecutively in Holton, Texas, and Oklahoma until 1916, when he became head of the health department at Kansas State College. He continued there until 1935, after which he practiced in Holton and Topeka. He was a captain in the medical corps of the Kansas National Guard from 1914 until 1918 and served on the Mexican border and again during World War I.

Clinicopathological Conference

Case Presentation

Dr. Francis N. Lorenz, resident in medicine: This is the first KUMC admission for this patient, a 58-year-old white male, whose chief complaints were a stroke and a lung condition.

He had been in good health except for a chronic, slightly productive cough until five weeks before admission. On July 22, he noted weakness of his left facial muscles, left hand, and left leg, without pain. There was no unconsciousness. He was hospitalized for 10 days and gradually developed some difficulty in talking. Gradual improvement of the weakness on the left side occurred. At dismissal from his local hospital on August 2, the patient could walk with ease but with an obvious left hemiplegic gait. The attention span was said to be poor, but the patient could talk coherently.

Spinal fluid examination done on two occasions at his local hospital showed no blood. X-rays taken at his local hospital showed some pathology in the right lung. It was largely for evaluation of his lung condition that the patient was referred to KUMC.

Approximately two hours before admission, while traveling to KUMC, the patient had a sudden episode in which his eyes became fixed, his color became gray, and there was profuse sweating. He vomited once and then felt somewhat better. Since then, it was his wife's impression that he did not use his right leg as well as previously. Also she noted a peculiar fixed stare in his eyes. He had more difficulty than previously in following instructions. There was no previous history of headache, dizziness, or syncope. There was no history known of hypertension.

The family history revealed one brother to have had moderately severe essential hypertension.

The system review was essentially noncontributory.

On physical examination, temperature was 100° rectally; blood pressure 100/70; pulse 84; respiration 20 and quite irregular. The appearance was that of an elderly male with a fixed stare; he seemed oriented as to time and place but had marked difficulty in following instructions. He would reply to questions with answers sometimes not revealing definite realization of the subject matter.

Head was symmetrical, without masses. The pupils of the eyes were small, regular, and equal, and responded to light and accommodation; the external ocular movements could not be tested because the patient could not follow instructions. It was the impression that the patient could not see. There was bilateral nasal haziness of both disc margins, more marked on the left. The pharynx was clear. The neck was supple.

There were increased breath sounds in the left base of the chest. The left cardiac border of dullness was within the midclavicular line in the 5th interspace. The sounds were of good quality; there were occasional premature contractions. A soft systolic apical murmur was heard but was not considered significant.

The liver, spleen, and kidneys were not palpable in the abdomen. No masses were felt.

There was definite weakness of the left arm and hand. The patient responded fairly well to instruction, but in general he seemed confused and restless. Vision was entirely absent in all fields as far as could be determined. There was left-sided facial weakness with some inability to close the left eye. The patient did not wrinkle the forehead on either side when instructed to do so. His tongue protruded in the midline. Reflexes showed hyperactivity throughout. There was hyperreflexia almost to the point of clonus in the reflexes of his left arm. Hoffman's sign was present bilaterally. No Babinski was present. Abdominal reflexes were absent. There was no ankle clonus.

Laboratory examination of the urine showed it to be acid, sp. gr. 1.019, having a faint trace albumin, no sugar, a few hyalin casts, 2 to 3 pus cells, and 1 to 2 red blood cells per high power field. RBC 4,980,000, hemoglobin 12.8 grams (83 per cent); WBC 11,600, of which 75 per cent were polys, all filamented, 13 per cent lymphocytes, 1 per cent basophil, 11 per cent monocytes. The platelet count was 150,000. On admission, NPN was 27.2, creatine 1.5, sugar 89, serum sodium 105 milliEquivalents per liter, potassium 4.1 mEq., chlorides 95 mEq. One week later NPN was 33, serum sodium 134 mEq., chlorides 98 mEq. On September 15, 1952, the day before death, NPN was 43 milligrams per cent, serum sodium 134 mEq., potassium 5.6, CO_2 21.8 millimols, chlorides 100 mEq. per liter. Cholesterol 388, with 67 per cent esters. Prothrombin time was 75 per cent of normal. Sedimentation rate showed a diagonal curve with a total fall of 3 millimeters in 60 minutes.

While in this hospital, the patient had irregular breathing characteristic at times of both Biot's and Cheyne-Stoke's respiration. The patient was extreme-

From the University of Kansas Medical Center. Edited by Glen R. Shepherd, M.D., and Mahlon Delp, M.D., from recordings of the conference participated in by the departments of medicine, neurology, pathology, radiology, and surgery (neurosurgery), and the third and fourth year classes of medical students.

ly restless, moving back and forth on the bed. The pulse was irregular at times, with bigeminy noted occasionally. The patient was given coramine and small amounts of barbiturate sedation for severe restlessness. Initially the patient took food and fluids fairly well. Marked confusion continued. Blood pressures were 140-150 systolic and 90-100 diastolic. The patient daily had a rectal temperature between 100 and 102°.

Because of his physical condition and confused state, it was impossible to do such further diagnostic studies as a bronchoscopy. Gradually increasing purpuric spots and later ecchymotic areas were noted over the arms, and some were also noted over the face. These were attributed to the patient's constant restless moving about in the bed. Gradually the patient became more restless, requiring greater amounts of intramuscular barbiturates and chloral hydrate. In the last 48 hours, the temperature rose to 103° on several occasions. Respiration became more labored and rapid. There was some dullness to percussion, and decreased breath sounds were present in the right posterior lung field. The day before death, the patient used his right leg much less than previously. On September 16, 1952, the patient expired.

Dr. Delp, chairman: Any questions concerning this history?

Q: Did this patient have a spinal tap while in this hospital?

Dr. Lorenz: No.

Q. Was the patient known to be right- or left-handed?

Dr. Lorenz: Yes, he was right-handed.

Q: Was a serology done?

Dr. Lorenz: No.

Q: What about the terminal episode?

Dr. Lorenz: He was responding enough to take some food and fluids about 9:30 a. m., and about two hours later he had developed cyanosis of the face and left arm with no obvious pain. Then he died.

Q: The history mentions a weakness in the left leg noticed before his admission here. Had that completely cleared up at the time of admission?

Dr. Lorenz: That was hard to evaluate. Probably there was some residual weakness. It was hard to evaluate because of his inability to follow instructions.

Q: Was the patient ever out of bed during the time he was here?

Dr. Lorenz: Yes, initially he was not incontinent. He would by one way or another let his wife know when he had to urinate and she could lead him to the bathroom. But he was out of bed only on those occasions.

Q: In this episode in the car while coming to KUMC, there definitely was no loss of consciousness?

Dr. Lorenz: Not as far as we could tell from his wife's story. There was just the profuse sweating and vomiting without unconsciousness or convulsions.

Dr. Delp: We have one electrocardiographic tracing on this patient. Mr. Culp, do you have that?

Mr. Louis Culp, fourth year student:* The EKG was essentially normal with premature systoles.

Dr. Delp: There are also x-ray studies on this patient. Mr. Claiborne, do you have those?

Mr. Richard Claiborne, fourth year student: PA view shows nothing abnormal in the thoracic cage. The heart is horizontal but seems to be within normal limits. There is nothing abnormal in the great vessels; there seems to be no shift of the mediastinum. The most striking feature is this area of increased density in what appears to be the right upper lobe. There is noted also increased infiltration throughout

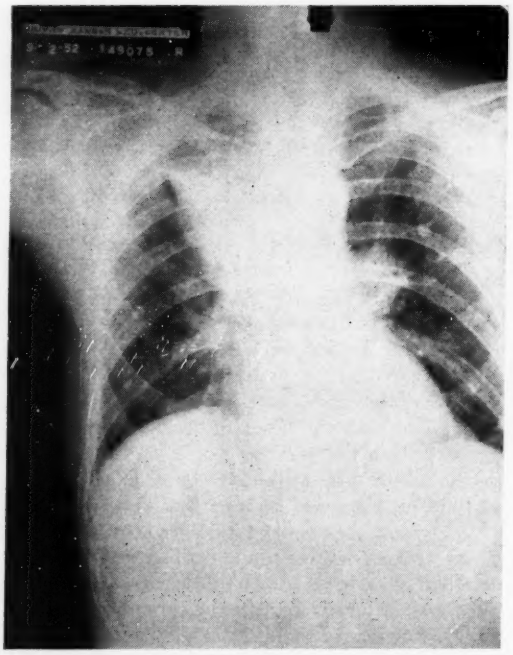

Figure 1. Chest x-ray showing increased density in right upper lobe suggestive of tumor mass or atelectasis, increased markings throughout right lung fields, left hilar shadow increased.

the right lung field as compared to the left. The smooth outline of the area of increased density would suggest the possibility of atelectasis, segmental atelectasis. I cannot rule out a tumor mass, but atelectasis would be my first choice. On the lateral view, you can see an area of increased density. This

* Though a medical student in March, 1953, when this conference occurred, he, like the others referred to as students, received the M.D. degree in June, 1953.

area is sharply demarcated here and would suggest to me the possibility of atelectasis, but I can't rule out tumor mass.

An incidental finding is this compressed vertebra. There is lipping of nearly all the vertebrae, with osteoarthritic changes. I believe these findings are of little importance since they probably produced no symptoms.

Dr. Galen M. Tice, radiology: That is a very good description. The question, of course, is whether this is a tumor mass or atelectasis? I agree with the student that there is a preponderance of evidence in favor of atelectasis. There perhaps is some displacement of the trachea toward that side to go along with it. Peribronchial infection in the right base would be consistent with partial obstruction and thickening of the bronchus and peribronchial infiltration due to retained secretions.

The compression of the vertebra I wouldn't pass off quite so lightly as of no significance. I think it is hard to tell sometimes if a compressed vertebra is of recent origin or if it has been there for a long time. Whether it has been there for weeks, months, or for years may be of some significance in relation to diagnosis.

I can't quite pass by the shadow in the left hilar area. Sometimes the pulmonary artery gives a confusing shadow there; this seems to be a little larger than the average pulmonary artery shadow in a man of this age. There was an increase in bronchial markings above it. That may be a mass in the left hilus. If it is, then that would bring other things into the diagnostic possibilities than we would consider if he had only an area of atelectasis on this side.

Dr. Delp: Mr. Baker, may we have your differential diagnosis?

DIFFERENTIAL DIAGNOSIS

Mr. Floyd Baker, fourth year student: We have here a 58-year-old male who was sent to this hospital primarily for the evaluation of pathology in his right lung found on x-ray studies. However, when the patient arrived at KUMC, his presenting symptoms were those of an intracranial lesion.

First of all, we would like to be able to locate the lesion in his brain, whether it was one focus or several. I want to attempt to describe a location that might explain most of his symptoms.

The original episode, that of weakness of the left side of the face, the left arm, and the left leg, would suggest a lesion in the cortical spinal tract, high up, probably in the cortex or in the internal capsule on the right.

There is some confusion about the second episode because of the difficulty in evaluating the eye signs and because of the entire condition of the patient. It is my impression that this patient probably was blind. This blindness would have to be due to a lesion at or behind the lateral geniculate bodies in the optic radiation, because of the reaction of the pupils to light. The optic radiation runs in the dorsal portion of the internal capsule; going more ventrally and laterally, you get to the arm and leg.

I think it entirely possible that the second episode, which was rather dramatic, could have been due to a hemorrhage with rapid extension across the midline, thereby involving both optic radiations and impinging a little upon the leg area in the internal capsule on the opposite (left) side.

There is just one catch—this man was right-handed and he had some difficulty in talking, and that would indicate that the lesion was in the left temporal region.

In the differential diagnosis one must consider a cerebrovascular accident. The original episode was not that of a hemorrhage. There was no previous history of hypertension. This episode was rather mild, of comparatively slow onset, not dramatic like that usually accompanying a hemorrhage.

An embolus, too, usually is more dramatic. This patient was not fibrillating; about 90 per cent of patients with cerebral emboli are fibrillating. The lung could be a possible source of a cerebral embolus, but that is uncommon.

The original episode was characteristic of cerebral thrombosis, with mild onset and gradual improvement. The second episode was not—it was more like a hemorrhage.

A brain abscess must be considered. We lack a history of any septic course of a previous infectious disease that might have been the source focus of a metastatic brain abscess. However, we still must consider that this might have been an old abscess with the original infection long ago. Usually, with brain abscesses, there are more encephalitis symptoms.

We have to consider tuberculosis because of the lesion in the lung. Usually, intracranial involvement from tuberculosis is more meningitic in character; we had no signs of meningitis in this patient. Also, there would be a more chronic course.

A brain tumor must be considered. A primary brain tumor usually has a more chronic course, with original symptoms of headache and visual disturbances. In the advanced stage there is marked papilledema. This patient did have early papilledema, but it was not marked.

As far as metastatic brain tumor is concerned—there is a very good possibility of a primary tumor in the lung, which is probably the most frequent one to metastasize to the brain. Metastatic brain tumors usually have a more acute onset and a more rapid course than primary brain tumors. This patient was

a male in the right age group for a carcinoma of the lung. He had a chronic cough. Frequently there is metastasis from carcinoma of the lung before there are many symptoms of the primary tumor.

If my localization is wrong, there is always the possibility that the patient had multiple metastases, which would explain the symptoms.

We always must consider the possibility of two diseases present in the same patient. For example, tuberculosis of the lung and cerebrovascular accident. But, whenever there is good evidence that the patient has one disease and all the symptoms may be explained on the basis of the one disease, I incline to that diagnosis until proved otherwise.

Therefore, my diagnosis is bronchogenic carcinoma with metastases to the brain. That vertebra doesn't appear to have had very much destruction, but there is the possibility of extension to the vertebra.

As for the cause of death—I feel that this patient died of pneumonia with probable respiratory failure. I think it should be mentioned that this patient was in respiratory difficulty all the time he was here. He was receiving heavy doses of barbiturates that might have had some effect on his respiration.

Dr. Delp: Mr. Blim, how do you account for these neurological findings?

Mr. Richard D. Blim, fourth year student: I think they are easiest to account for on the basis of diffuse multiple metastases. If I had to pinpoint them, I would pick the internal capsule, but that doesn't explain the aphasia or confusion the patient had. Some of the confusion could have been due to the chloral hydrate or the barbiturates he was receiving.

Dr. Delp: Mr. Black, how do you explain this patient's fever? He had fever at the time he arrived; he had fever each day he was here.

Mr. Don Black, fourth year student: I can't explain why he had fever when he arrived. He had fever while here probably because of aspiration of fluids.

Dr. Delp: Mr. Battin, do you have any suggestions?

Mr. Keith Battin, fourth year student: I think probably the fever was due to a pneumonic process.

Dr. Delp: Mr. Altman, do you think the patient had a metastatic disease of the brain?

Mr. Harold Altman, fourth year student: I think you probably could explain part or all of his terminal fever on the fact that he was extremely restless and was moving around so much.

Dr. Delp: Do you think that he had metastatic disease of the brain?

Mr. Altman: Yes.

CLINICAL DISCUSSION

Dr. Delp: We are going to ask Dr. Steegmann and Dr. Brackett to localize the central nervous system lesion for us. You might comment on the etiology, too, if you care to. Dr. Steegmann?

Dr. A. T. Steegmann, neurology: I do not find the localization easy in this case. We are more or less forced to assume that probably there was a lesion on both sides. I feel that the symptoms point more to a lesion in the right frontal region, involving the motor portion of the hemisphere, because there was left-sided weakness. The patient had also what I feel was hemianopsia, but it is difficult to delineate that because of the difficulty in examining the patient.

After thinking it over and after seeing the patient, I decided that this so-called blindness probably was an apperceptive blindness—what sometimes is spoken of as Pick's blindness—which really is a form of disorientation. It is not actually due to an involvement of the visual pathways but is an involvement of the associational visual mechanisms. These patients appear to be blind, they are not actually blind. That, of course, would carry with it the thought that there might have been a lesion in the parietal lobe, perhaps on either side, but probably in the dominant hemisphere. The patient was right-handed, if I am not mistaken.

Then the appearance of symptoms referable to the right side brought up the question of whether there was a lesion on the opposite side, also. It was my opinion, in view of the changes in the lung, that this probably was metastatic, but there was one difficulty. That was the relatively sudden onset of symptoms. So I changed my mind as to possible metastasis and ended up my consultation note, on the first consultation, by being a bit more conservative and saying that it might be a vascular lesion.

I still think the question of precise localization in this case is difficult. I would like to make one comment about the question of localization. There is a difference between localization of a hemiplegia secondary to an occlusion of the sylvian artery and a hemiplegia from the internal capsule. I notice that students frequently speak of a hemiplegia from the internal capsule in the same sense that they speak of a hemiplegia from an occlusion of the branches of the sylvian artery distal to the perforating branches. The hemiplegia due to a lesion in the perforating branches is always symmetrical, being equally in the arm and leg, is spastic in type, and is not associated with any aphasia or aphasic disturbances.

On the other hand, if the lesion is in the distal portions, encroaching upon the sylvian artery distal to the perforating branches, then the hemiplegia is of arm-and-aphasia type. It is much more pronounced in the arm than in the leg.

If it is a hemiplegia involving the perforating

branches, encroaching somewhat on the island of Reil but not affecting the superficial branches in the cortex, then the hemiplegia is symmetrical but usually flaccid. Those are important differential diagnostic ideas that I think everyone should know. It only means that you must know a little about the blood supply in the brain to understand it.

Dr. Delp: Dr. Brackett?

Dr. Charles Brackett, neurosurgery: I think Mr. Baker regarded the first episode just right and that the patient had an involvement of the cortical spinal tract, the cortical bulbar tract, somewhere above the 7th nerve nucleus. That's about all you can say as to localization of the first lesion.

In the hospital he was thought to be blind. This would imply one of two things: he had bilateral occipital lobe lesions or lesions of the radiations. That could not be a simple lesion; it was bound to lie in two separate structures. Or he had a lesion in the left parietal-occipital area (being plainly right-handed) so that he had a visual agnosia—did not recognize what he saw.

But to be perfectly correct, I believe it was in the lateral geniculus because he had a light reaction from it.

And, finally, when he died, he did have weakness of the right leg. So I note that the patient had evidence of three localizations: right frontal, left parietal-occipital, and possibly the brain stem.

As to the nature of the process—this patient awoke in the morning with a left facial paralysis which gradually progressed over a period of hours to involve the arm and the leg. He had no hypertension, he had no headache, no unconsciousness, no evidence of increased pressure; and the spinal fluid was normal on several occasions. So I think this was clearly an episode of thrombosis.

The second episode, on the way in to KUMC, probably was not a thrombotic episode.

The main problem in the case is the differential diagnosis between metastatic carcinoma from the lung and cerebral thrombosis. There is nothing in the history to suggest embolization.

Metastases from the lung are embolized. They may produce a sudden onset occasionally, due either to an embolization or to hemorrhage from the tumor. But I think it would be extremely unlikely for three such episodes to occur. Furthermore, following each episode there was significant improvement, so our conclusion was that this patient was suffering from cerebral thromboses unrelated to his chest pathology.

Dr. Delp: Dr. Schloerb, with the history, ignoring the neurological findings and the other physical findings, plus this x-ray film, do you believe the patient had a carcinoma of the lung?

Dr. Paul Schloerb, surgery: Yes. One question that comes to my mind: He did develop purpura during the course of his hospital stay, and I wonder if that was evidence in favor of there being hemorrhage into the cerebral metastasis? Was that purpura studied in terms of bleeding time and clotting time?

Dr. Lorenz: The patient did have a normal prothrombin time. No other studies were made.

Dr. Delp: Dr. Berry, assuming that this is a carcinoma of the lung, did this patient die of the carcinoma of the lung?

Dr. Max Berry, medicine: No, I don't think so. He had fever all the time. That, of course, is sometimes a complication of the cerebral lesions, but it should have been a little higher than that.

Dr. Delp: Do you believe this patient had carcinoma of the lung with metastasis?

Dr. Berry: To the brain? It is awfully difficult to explain it otherwise, because of three things. First, he was well until he started out with these brain episodes, except for a chronic cough which nobody made much fuss about. The second thing is that he had a lesion in his lung. We can see it on the x-ray film. It probably was atelectasis, with bronchial obstruction due to the tumor. The third thing is, he had three different localizations in his brain which would mean that something could be seeding from the lung.

Now, carcinoma is one of the things it could have been. And the other thing that it could have been was an abscess or infection in his lung.

But he had a lesion in the back with a crumpled vertebra, and with all those things tying together, you are forced to make a diagnosis of carcinoma of the lung.

Dr. Delp: Dr. Allen, why did this patient have fever?

Dr. Max Allen, medicine: We thought his fever was due to the lesion in his lung—atelectasis and probably bronchial pneumonia and perhaps abscess formation back of the obstruction in the lungs.

Dr. Delp: Is there anyone in the audience who would like to volunteer a statement as to why this patient had fever, and what the lesion was in the brain? Dr. Rankin?

Dr. Thomas J. Rankin, medicine: There is one thing I would like to know. What was the pulse rate?

Dr. Lorenz: It was not phenomenal; it was 84 on admission.

Dr. Rankin: I must go along with the majority and say that I thought this patient had carcinoma of the lung with metastasis to the brain. However, I feel that the possibility of a metastatic abscess to the brain from pulmonary infection has not been given enough consideration.

Before the present frequent use of antibiotics, I

have seen such cerebral abscess formation from pulmonary disease fairly frequently. Since the antibiotic era, this has not been my experience.

Dr. Delp: How many people think this man had a carcinoma of the lung? How many think he had metastatic carcinoma of the brain? Does anyone think he had any other sort of metastatic disease of the brain?

Dr. Rankin is the only one who suggested that he had an infectious metastatic lesion, I believe.

Dr. Charles C. Herbert, medicine: The possibility of multiple emboli to the brain is suggested by the clinical picture. The question is the source. The description of the heart suggests a normal heart, so we have no evidence from what we have been given to indicate that he may have had an endocarditis. It is usually a hidden disease in old men, or it can be. The fact is that there has been so much talk about the cause of the fever that I am beginning to suspect the rare.

Dr. Delp: Dr. Frenkel, may we have the pathology report?

PATHOLOGY REPORT

Dr. Jacob K. Frenkel, pathology and oncology: Autopsy demonstrated the occurrence of two lesions, both rather rare. As was suspected, this patient had a carcinoma of the lung. However, the carcinoma was not well seen grossly and looked very much like pneumonia. It extended through both lobes, and there was considerable discussion at the time of autopsy as to whether this was carcinoma or whether it was pneumonia.

We will see from its microscopic appearance that the lesion was a relatively unusual one, and that it somewhat resembled both alveolar cell carcinoma and pulmonary adenomatosis in that the distribution of the carcinoma followed the alveolar lining cells.

The second lesion that was found grossly was a lesion on the mitral valve, a form of endocarditis not associated with bacteria, so-called nonbacterial verrucous endocardiosis. This lesion, to my knowledge, does not commonly give rise to emboli. In a survey of some 50 to 75 cases in the literature, no emboli are mentioned. However, Dr. Pollack informs me that she has seen one or two cases where emboli were present. Emboli from the mitral valve, nonseptic emboli, give rise to infarcts in the brain, heart, and kidney.

The lesions in the brain had their distribution in both the left temporal and the right occipital lobes, and in both the posterior and the central gyri of the brain. The patient also had bronchopneumonia.

Microscopic: As we see on this slide, the patient had a carcinoma with papillary as well as squamous components. The predominant form is the papillary type. This resembles somewhat an infectious disease of sheep, jaagsiekte, thought to be due to a virus. This disease is endemic in sheep and, in at least one instance, pulmonary adenomatosis has been found in a woman who had spent some time on a sheep ranch where that disease was prevalent. No such association is recorded in the history of our patient; his occupation was that of brickmason.

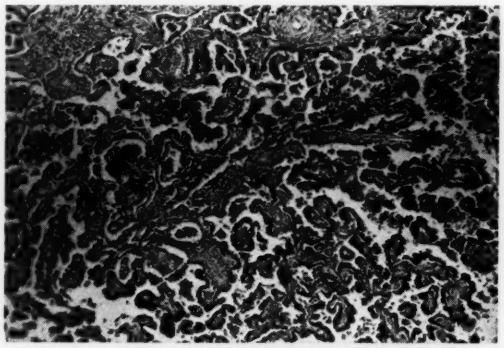

Figure 2. Lung with papillary carcinoma predominating; some squamous areas are also present. Magnification x(92).

This tumor might be classified also as an adenocarcinoma of the lung, because the tumor cells resemble the cells of the small bronchioles. No mucus was found. Pulmonary adenomatosis is often multicentric in origin, and papillary bronchogenic carcinoma can be likewise. The presence of diffuse involvement of the lung may also be explained by the occurrence of metastasis throughout the lung.

This next slide shows a case of pulmonary adenomatosis from the woman referred to. The following slide shows a lesion found in the lungs of a sheep with which this woman had been associated.

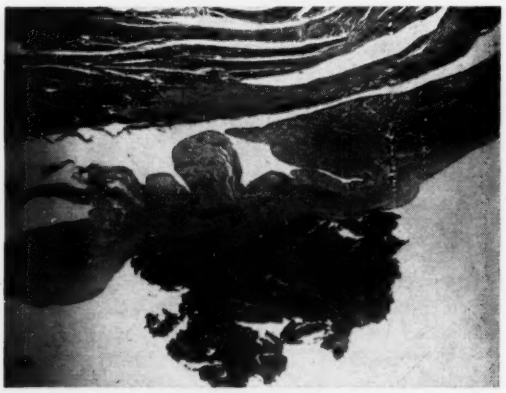

Figure 3. Mitral valve with vegetation, composed of fibrin and platelets. Note the absence of bacteria and leukocytes. Magnification x(25).

Here we see the lesion of the mitral valve; here is the valve leaflet. The entire lesion has been sec-

tioned so it is missing from the gross specimen. Here is the thrombotic projection, the verruca, on the valve. You will notice its uniform appearance and the absence of bacterial colonies such as are found frequently with bacterial endocarditis.

Here we see a lesion in a cerebral vessel showing embolic material, and a focus of softening in the adjacent brain. In the heart, the embolus of the non-bacterial type results in an infarct.

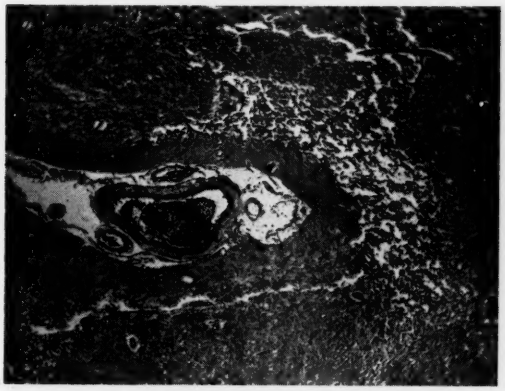

Figure 4. Brain showing organizing embolus in vessel and adjacent area of infarction. Magnification x(55).

In summary, we saw a concurrence here of two fairly rare lesions, producing a rather bizarre picture in this patient who puzzled us very much.

Dr. Delp: Any questions of Dr. Frenkel?

Dr. Tice: Was there pathology in the left lung?

Dr. Frenkel: Yes, the tumor was in both lungs, and it was alveolar in distribution; bronchopneumonia likewise was present.

Dr. Berry: Did you examine that dorsal vertebra that was compressed?

Dr. Frenkel: It was examined. It seemed to be the result of an old fracture. It did not contain metastatic tumor.

Dr. Robert Bolinger, medicine: Dr. Frenkel said that there was embolus in the coronary artery. How did he know whether it was embolus or thrombosis?

Dr. Frenkel: The appearance of the thrombus suggested that it arose as an embolus.

Q: Were there lesions in the hypothalamus?

Dr. Frenkel: No.

ANATOMICAL DIAGNOSIS

Primary: Papillary bronchogenic carcinoma of the upper lobe of the right lung with metastases to the lower and middle lobes of the right lung and both sides of the left lung.

Bronchopneumonia of the lower lobe of the right lung and both lobes of the left lung.

Non-bacterial verrucous endocardiosis of the mitral valve with embolic occlusion of small branches of the coronary arteries and multiple small infarcts of the myocardium.

Multiple infarcts of the left kidney, of the left temporal and right occipital lobes, and of both posterior central gyri of the brain.

Focal fatty metamorphosis of the liver.

Accessory: Arteriosclerosis of the right circumflex and left anterior descending coronary arteries, advanced; of the left circumflex coronary artery, slight; of the cerebral arteries, slight to moderate; of the aorta and the pulmonary arteries, slight.

Sclerosis of the bases of the cusps of the mitral and aortic valves.

Fibrous thickening of the appositional surfaces of the mitral valve and of the tricuspid valve, slight.

Chiari's network, right atrium.

Hypertrophy and dilatation of the heart (400 grams—formalin-fixed).

Focal fibrosis of the myocardium of both ventricles.

Chronic passive congestion of the liver and of the small and large bowel.

Multiple ecchymoses of the mucosa of the small and large intestines.

Hydropericardium (50 ml.).

Fibrosis of the spleen.

Scar of lower pole of right kidney.

Cysts of right kidney, small.

Absence of the teeth.

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There seems to be little doubt that physical and intellectual fatigue, as well as painful emotions, decrease resistance of the body to infection; but the physiologic mechanisms which determine these important relationships are totally unknown. Despite all this ignorance, however, a belief shines as a beacon to guide our efforts. It is that the defense mechanisms of the body which promote resistance to infection appear to be closely related to the physiologic processes which make for good health—good health being here measured in the terms broadly referred to as well-being by the layman. The inner logic of the program of antituberculosis associations should lead them to become truly health associations. For it can hardly be doubted that, in final analysis, health is a positive attribute rather than merely the absence of disease.—*Rene J. Dubos, Ph.D., Am. Rev. Tuberc., July, 1953.*

The Cerebral Circulation: Comments on Cerebral Angiospasm

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I. INTRODUCTION

The cerebral circulation is certainly not a new phase of physiology, but one that has been the subject of investigation for more than a century.[22] The literature on this subject is quite voluminous, especially in the past 25 years. World War II brought about a great increase in man's knowledge of cerebral circulation due to its importance and application to the field of military activity, particularly that of high-speed, high-altitude aviation. The year 1944 marked a symposium on the cerebral circulation,[1, 4, 10, 22] an evaluation of the then current status of cerebral circulation.

Here, Schmidt noted, "The most important human strains of combat flying are related to anoxia, aeroembolism, cold, acceleration, motion sickness, disturbances of the special sensory apparatus, fatigue, and psychic deterioration. This list is not likely to require substantial modification when more recent experience is disclosed. Now it is a striking fact that the brain is the limiting factor with respect to all these strains, either because its functional capacity is reduced (as by anoxia, cold, or the cerebral anemia or congestion associated with acceleration), or because it is subjected to an intolerable bombardment by sensory nerve impulses (as in the pain of decompression sickness, the nausea of motion sickness, the discomfort of cold, or the accumulated psychic trauma associated with combat aviation). The blood supply of the brain then becomes a matter of immediate concern, not only because here, as elsewhere in the body, the capacity of the tissue to function is limited by the capacity of its circulation to meet its changing requirements, but for the additional special reason that the brain is unable to contract much of an oxygen debt and therefore is more subject than other tissues to derangement by an insufficient supply of blood."

Recent advances in neurosurgery have also stimulated the need for more knowledge of the cerebral circulation.

Since the symposium in 1944, new experimental techniques have greatly added to our knowledge of the circulation of the brain. The nitrous oxide method of Kety and Schmidt has opened a whole new phase of investigation, produced much additional information, and promises more in the near future.[2, 9, 13, 14, 15, 16, 17, 23, 25, 26]

It is the purpose of this paper to discuss briefly the cerebral circulation, with some comments on cerebral angiospasm.

II. ANATOMY—GROSS

The general arrangement of the cerebral vessels is quite constant in different mammals although the details show wide species variations.

Arterial:[23] The arterial supply of the brain is derived from the carotid and vertebral arteries, the main branches of which fuse at the base of the brain to form the circle of Willis. From this arise three pairs of arteries (anterior, middle, and post cerebral) which course over the convex surfaces of the cortex above the tentorium and send smaller branches into the brain substance constituting its main supply of blood. The basal ganglia and choroid plexus are supplied by a few direct branches. The anterior spinal artery forms an anastomosis with the vertebral-basilar system which is functionally insignificant in man but may be of considerable importance in some animals (particularly dogs).

The size of the primary arteries to the brain, and hence the importance, may vary considerably in different species. Thus the carotids are practically the exclusive supply of the brain of the ox and goat. In the lemur, the carotids are rudimentary and the vertebrals are the main source of blood supply. Man is intermediate in this respect, and both carotids and vertebrals are important in supplying blood to the brain. The monkey is similar to man in this respect. The rabbit is the only common laboratory animal in which the main supply of the circle of Willis is the internal carotid. The main supply in the dog and cat is a complex anastomosis between the orbital distribution of the external carotid and the internal carotid just before it enters the circle of Willis. Here, the internal carotid is relatively insignificant until just before it enters the circle inside the skull.

The significance of these anatomical arterial variations is far-reaching in experimental attempts to measure cerebral arterial flow by means of instru-

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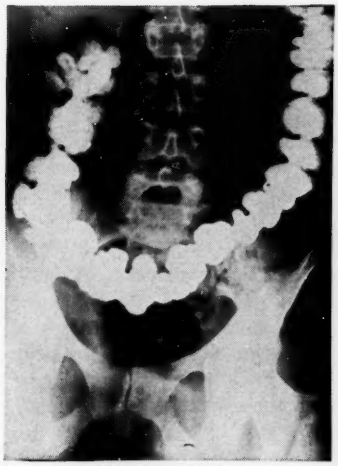
This is one of 11 theses, written by fourth year students at the University of Kansas School of Medicine, selected for publication by the Editorial Board from a group judged to be the best by the faculty at the school.

Thesis written while the author was a fourth year student. Dr. Mansfield is now interning at U. S. Army Tripler General Hospital, Honolulu, Hawaii.



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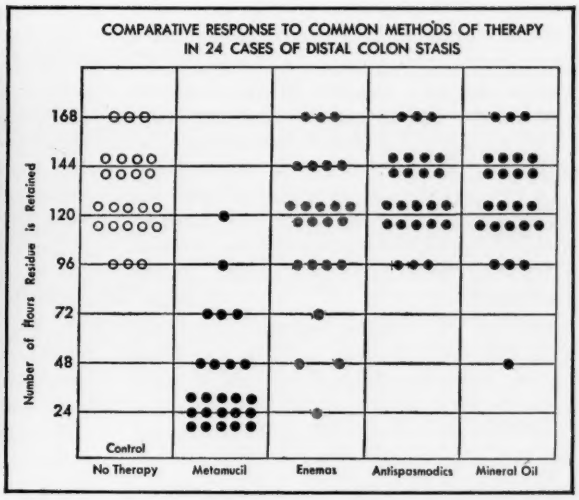

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*Barowsky, H.: A Roentgenographic Evaluation of the Common Measures Employed in the Treatment of Colonic Stasis. Rev. Gastroenterol. *19*:154 (Feb.) 1952.

ments applied to the carotid and/or vertebral system. In this procedure it is necessary that all communications between the intra- and extracerebral distributions of these vessels be closed, otherwise there is no way of determining whether changes in flow are due to the intracerebral or the extracerebral systems.[23]

The brain in man is supplied by blood entirely by means of the internal carotids and vertebrals. There is no significant anastomosis with extracerebral arteries as exist in lower mammals. The carotids supply (in general) the anterior and middle portions of brain on each side. The basilar artery (formed by the vertebrals) supplies the occipital lobes, portions of the temporal lobes, and the structures of the posterior fossa.[13]

By means of dye injection techniques in living human subjects, there is good evidence that blood entering the brain via each internal carotid artery is distributed almost wholly to the ipsilateral hemisphere and drained predominantly by the corresponding internal jugular vein.[24] There is also good evidence that blood in each jugular is fairly representative of the drainage from all histological components of the brain. Blood obtained from the superior bulb of the internal jugular vein is relatively free of blood derived from extracerebral sources.[24] However, surgical procedures involving the ligation of the carotid[26] have demonstrated the potential contralateral arterial supply in human beings.

Venous:[23] The venous return from the brain is accomplished through vessels of three groups—superficial cerebral veins, deep cerebral veins, and cerebral venous sinuses. The superficial cerebral veins empty mainly into the superior longitudinal and lateral sinuses; several larger channels empty into the superior sagittal sinus. The deep cerebral veins are gathered into the paired internal cerebral veins which unite to form the great cerebral vein (Galen) which drains into the straight sinus. The cerebral venous sinuses are clefts in the dura mater and are devoid of elastic and muscle tissue ordinarily seen in veins; the most important of these are the unpaired superior and inferior sagittal sinuses, the paired lateral sinuses, the unpaired straight sinus, the paired cavernous sinuses, the occipital sinus. Five of these (the superior sagittal, straight, occipital, and the two lateral sinuses) usually unite at a point directly under the external occipital protuberance to form the torcular Herophili.

Venous blood leaves the brain mainly by the jugulars, into which the torcular and cavernous sinuses drain directly. There are also communications with the veins of the spinal canal, which are arranged as anterior and posterior plexuses communicating at each intervertebral space with the vertebral, intercostal, and lumbar venous systems. The small emissary veins communicate directly between the cerebral sinuses and the extracerebral venous system of the head.

The major venous return from the brains of primates and man is through the internal jugulars, although the external jugulars also carry appreciable amounts. The converse is not true: the blood in the superior jugular bulb is contaminated only with negligible amounts (average 3 per cent) of blood derived from extracerebral tissue. It is important to note, however, that once the large common facial vein enters the internal jugular this is no longer the case.[23]

The Munro-Kellie Doctrine:[23] The Scotch anatomist, Munro, formulated the conception that since the cranium is a rigid, indistensible box completely filled with incompressible contents, the quantity of blood contained within it cannot change appreciably. Kellie supported this hypothesis 40 years later by experiments and autopsies.

The significance of this hypothesis is that it has several important consequences. Increase in the volume of any one of the contents of the cranium will be at the expense of the others. The most labile of the contents being cerebrospinal fluid (CSF) and blood, one or both of these will be displaced by increase of normal or abnormal tissue in the skull. Also an increase of the CSF pressure is transmitted equally throughout the system, and, once it surpasses the pressure in the cerebral blood vessels, they will collapse until their pressure is at least equal to that exerted on their walls. Since the intravascular pressure is lowest in the veins, as long as there is an outward flow of blood the venous pressure must equal that of the CSF, and an increase in CSF pressure will be accompanied by an increase in venous pressure. A venous pressure rise will also result in a rise in CSF pressure.[23]

Anatomical problems:[1] Organs with pedicles through which the major blood vessels enter and leave are the most favorable for the study of blood flow. This is not so with the brain, for here the blood supply is quite complex and there are a number of anastomoses.

If the rate of flow is to be measured on the arterial side, an experimental animal is required in which it is possible to include all the blood going into the brain and exclude all going elsewhere.

That the vertebral vein plexus is of considerable importance is shown by Batson[1] in a case of total occlusion of the superior vena cava where the patient's only complaint was a swollen face. Here it must be admitted that the plexus must have been a functioning system in order to be able to take over in the face of this emergency.

Some animals have a peculiar elaboration of vessels known as a rete mirabile. This network provides

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intra- and extra-cranial junctions between the cerebral vessels and the external carotids. These animals are unsuited for studies of cerebral arterial flow. The Rhesus monkey does not have a rete mirabile. Here, for practical purposes, the anatomy approximates that of man. The cat and dog are not suitable because of retes.

Of the animals reviewed (cat, dog, monkey, rabbit), the venous side is unsuited in all for the study of the cerebral blood flow.

Histological anatomy: The morphology of the cerebral blood vessels differs from that of the blood vessels of the visceral organs. The intima is separated from the media by a distinct, elastic membrane which is better developed here than in the blood vessels elsewhere in the body.

The media likewise contains a few elastic fibers irregularly scattered and intimately mixed with the circularly-arranged muscle fibers. No external elastic membrane between media and adventitia is present in cerebral blood vessels. The adventitia consists of loose connective tissue, the nuclei of which are parallel to the axis of the blood vessel. There is a lack of elastic tissue in the poorly developed adventitia.[21]

The elastic tissue of the cerebral vessels is thus segregated into a well developed layer which is relatively rigid, and it is surrounded by a smooth muscle layer, probably devoid of elastic tissue. This muscle layer, in turn, is surrounded by a sponge-like perivascular space which, too, is non-rigid. This arrangement is in contrast to the blood vessels in skeletal muscle, for example, where the elastic tissue is interspersed throughout the blood vessel walls, thus affording comparatively slight shock absorbing quality.[21]

The Virchow-Robin perivascular space, a typical feature of the cerebral vascular system, is a structure of pathologic importance.[21] It may be looked upon as a loosened adventitia lined with flattened connective tissue cells. This space becomes visible under pathologic conditions, for normally it is collapsed and shrunken. The Virchow-Robin space is peculiar to the central nervous system, apparently taking the place of a lymphatic system, for there are no separate lymphatic vessels in the brain or spinal cord.

The space of His outside the adventitia is considered generally as an artifact. The space of Held is an area of tissue rarefaction in the parenchyma of the brain.

In regard to perivascular nerves, Humphreys[12] in 1929 demonstrated by histologic techniques a rich perivascular nerve supply in nearly 100 per cent of the intra-cerebral vessels impregnated. These vessels were of all calibers down to 10 microns. Fiber counts gave an estimate of this rich supply. He believed these nerves to be autonomic and vasomotor—both sympathetic and parasympathetic. This is discussed in more detail later.

III. PHYSIOLOGY

There is now a mass of unequivocal evidence from experiments on animals to indicate that the blood vessels in their brains are subject to all the influences that affect the circulation elsewhere in the body, viz., vasoconstrictor and vasodilator nerve impulses, metabolic products, hormones, and drugs. A smaller amount of evidence indicating that some of these relations also exist in man has become available very recently and more is to be expected in the near future.[23]

Blood pressure: In general the cerebral circulation tends to follow passively the changes in arterial pressure, even to a greater extent than most other organs; however, it probably has a greater capacity for resisting or compensating such changes than has been suspected in the past.[23]

According to Kety,[13] the rate of cerebral blood flow depends on two factors: (1) blood pressure head, and (2) cerebrovascular resistance, each of which may be influenced by a variety of factors. His work does not substantiate the earlier belief that cerebral blood flow passively follows changes in arterial blood pressure. "The cerebral blood flow is, above a critical minimal arterial pressure, regulated intrinsically. The critical minimal arterial pressure is probably not far below the normal mean pressure, as indicated by the cerebral symptoms associated with orthostatic hypotension. Above shock levels of blood pressure the cerebrovascular resistance is the predominant regulator of the cerebral blood flow. Cerebrovascular resistance is the resultant of all factors tending to impede the flow of blood through the brain and includes intracranial pressure, blood viscosity, and organic changes as well as the functional tone of cerebral vessels."

Vasoconstrictor nerves: Forbes and Wolff[7] furnished the first unequivocal demonstration of constriction of cerebral blood vessels resulting from the stimulation of sympathetic nerves. This was done by microscopic observations and measurements of the surface vessels of the parietal cortex of anesthetized cats. These decreases in vessel diameter were in the order of 10 per cent or less, whereas corresponding decreases in dural vessels were about 30 per cent and those of the skin 80 per cent. The cerebral effects were obtained by stimulation of the ipsilateral cervical sympathetic nerve.

No effects were obtained by stimulation of fibers of the stellate ganglia and the vessels of the vertebral arteries. Cervical sympathetic cerebral vasoconstrictor innervation has been demonstrated also, by C. F. Schmidt et al. in a series of papers, by means of

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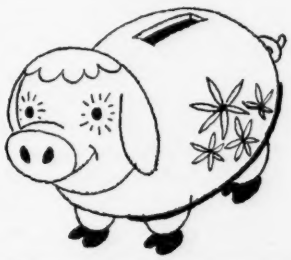

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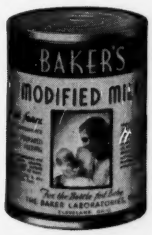

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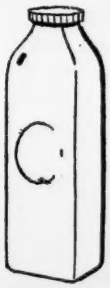

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a thermo-couple inserted in the hypothalamic region and parietal cortex of the cat and the parietal cortex of the rabbit. However, the same method revealed no sign of innervation in the medulla, pons, and occipital cortex of the cat. This made evident that generalizations of the cerebral circulation as a whole could not be drawn from observations on only one part of it, and that it would be necessary to obtain data of the behavior of the cerebral circulation as a whole. This was done by direct measurements of the cerebral arterial inflow in monkeys, and no significant reduction in cerebral flow was obtained by sympathetic stimulation strong enough to produce mydriasis and salivation.

The possibility of cerebral angiospasm from sympathetic impulses or from intrinsic vasoconstrictor innervation with or without extracranial connections can neither be affirmed nor denied, according to Schmidt,[23] but at present the evidence is against it.

Vasodilator nerves: One of the most important peculiarities of the cerebral circulation is that its vessels can be dilated strongly by many influences, constricted weakly by only a few; the best available conception of its intrinsic control is that it is dilator rather than constrictor in direction.

The first definite evidence of cerebral vasodilator innervation was demonstrated by means of the pial window, as was vasoconstrictor innervation, and this is mediated by nerve fibers passing from the facial nerve through the geniculate ganglion by way of the superficial petrosal nerve to the pericarotid plexus.[3] Other pathways such as the vagodepressor nerve and the carotid sinus nerves have been claimed to be cerebral vasodilators; however, the evidence for this is apparently not well founded.[23] The significance functionally of the first mentioned paths is not yet known.

Metabolic products: In general, as with the other vessels in the body, the cerebral vessels are dilated by all the usual products or consequences of metabolism. This includes decreased oxygen, increased carbon dioxide, increased acidity, increased temperature, as well as a number of other agents such as acetylcholine, histamine, potassium, and calcium ions which are now associated with cellular activity.[4, 13, 23, 25] There is also cerebral vascular constriction produced by reverse metabolic changes such as increased oxygen and decreased CO_2. Decreased CO_2 is probably the most potent cerebral vasoconstrictor yet found and used under physiological conditions. In this respect the cerebral vessels are unique. Schmidt[23] believes that the degree of dilatation in severe anoxemia in man would be nearly equal to that of increased CO_2, although the effects of severe anoxemia (i.e., less than 10 per cent O_2) have not yet been studied. Schmidt also believes that the behavior of the cerebral circulation under physiological as well as pathological conditions is influenced more by metabolic agents than by any other factor.

It has been known for some time that acids dilate the cerebral vessels and alkalis produce constriction. These changes, however, are not as marked nor as consistent as changes produced by variation in CO_2 tension. The most pertinent evidence has been obtained recently in studies on patients in diabetic acidosis. Here the cerebral blood flow apparently decreases with arterial CO_2 tension over the arterial pH range 7.40 to 7.10. When the acidosis becomes more severe than pH 7.10, cerebral blood flow tends to increase sharply, the curve of its behavior being very similar to that portraying pulmonary ventilation.[17] This is consistent with the belief that CO_2 tension is the dominant influence in regulating both the tone of cerebral vessels and the activity of the respiratory center over the ordinary physiological range. Beyond this, however, other agents may overrule the normal regulator.

Hormones: Wiggers, as far back as 1905, demonstrated in the perfused isolated dog's brain the vasoconstriction response and diminution in the perfusion flow to epinephrine, when it was added to the perfusion fluid. That epinephrine can constrict the cerebral blood vessels has been confirmed by many other investigators using various techniques on dogs, cats, and monkeys. However, there is general agreement that the effect on cerebral vessels is so much weaker than that on vessels elsewhere, that the cerebral vessels will be passively dilated whenever epinephrine is distributed uniformly throughout the body. Thus epinephrine, given systemically, will only increase cerebral blood flow, dilate cerebral vessels, and exaggerate any existing tendency to cerebral hemorrhage.[6, 23]

The results of pituitrin and pitressin studies in animals indicate no direct effects upon the cerebral circulation. The effects of angiotonin or hypertension should be interesting but have not yet been demonstrated.

Drugs: Among the vasodilators a large number of drugs may be capable of cerebral-vasodilatation. For example: the nitrites, choline derivatives, the xanthine group (caffeine, theophylline, theobromine), histamine, the opium alkaloids (morphine, codeine, papaverine), the entire group of narcotics and anesthetics, and calcium and potassium ions are included in this large group. Since, however, the intracranial vessels are generally less sensitive to these drugs than the extracranial vessels, a drug concentration high enough to act all over the body would probably bring about a redistribution of the blood at the expense of the brain and a reduction in the cerebral blood flow. Carbon dioxide may be mentioned as an

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outstanding exception to this, for here the vasomotor center is stimulated while the cerebral blood vessels are dilated.[23]

Shenkin,[25] using the nitrous-oxide method of Kety and Schmidt,[16] has studied the effects of caffeine, papavarine, histamine, and benzedrine upon the cerebral circulation of man. These recent experiments have shown that caffeine produces increased vascular resistance, a reduced cerebral blood flow (15.6 per cent), and little change in cerebral O_2 consumption. Papavarine produced significant vasculature relaxation but reduced the mean arterial pressure so that the cerebral flow was not significantly increased. Benzedrine did not produce any marked effects. Histamine, however, proved to be an excellent cerebral vasodilator, causing an increase in the cerebral blood flow when the general arterial pressure was reduced as much as 15 per cent. Greater reduction in the arterial pressure caused proportional reduction of the cerebral circulation. Furmanski[8] has shown clinically in a series of 25 patients with brain ischemia due to thrombosis, embolism, etc., that 20 responded with definite improvement to intravenous histamine therapy. (Histamine diphosphate 2.75 mg. per 500 cc. isotonic fluid I V over two hours.)

The strongest vasoconstrictor of the cerebral vessels yet demonstrated is that of decreased CO_2 tension. Recent investigations, using the nitrous oxide technique,[13, 27] have shown that aminophylline given intravenously in therapeutic dosage in man produces a constant cerebral vasoconstriction, a significant reduction in cerebral blood flow, and a resultant cerebral anoxia. It has also been shown that dihydroergocornine causes a release of cerebrovascular resistance in patients with essential hypertension and to a lesser extent in normal subjects.[11]

IV. EXPERIMENTAL TECHNIQUES[10]

Changes in pial vessels: Changes are usually observed only in local areas, and this also does not necessarily portray the picture of what is going on in arterioles deep in the cerebral tissue. Also these observations may not always apply to the unanesthetized animal.

Perfusion technique: Here the cerebral flow is maintained by a mechanical pump, and the observations are made under unphysiological conditions.

Measurement of flow by instruments attached to vessels: If measurements are made on one vessel, the others being untied, they may or may not record directional changes correctly. If all other arteries are tied, the specimen becomes unphysiological.

Measurement of blood flow in the intact blood vessel: There are many instruments used, such as thermostromuhrs, etc., and here the many technical variables are difficult to control.

Measurement of blood flow with thermoelectric instruments: Here again are many variables which are difficult to control. The method is not specific and is not quantitative. There are too many sources of error.

Cerebral AV O_2 differences: These have been used as an index of cerebral metabolism. This method does not take into account extra-metabolic factors which may alter the rate of cerebral flow and consequently change the AV O_2 difference. Here again the variables are not brought into control. This method has also been used as a measure of cerebral blood flow, assuming the cerebral metabolism as constant, an assumption which for these purposes is not justifiable.

Plethysmographic method: This method involves the use of a cuff about the neck, at a pressure of 60-80 mm. Hg. in order to stop venous return. Here it is assumed that the CSF is displaced, is proportional to the cerebral flow, and can be measured by the rate of CSF flow through a lumbar needle. According to Gregg and Shipley,[10] the venous outflow from the cranium is not halted by this procedure.

With the exception of the perfusion experiments, all of the preceding procedures have involved making observations from which the magnitude of, or directional changes in blood flow are determined only indirectly. In order that any direct method be considered valid, it is necessary that (1) the available quantity actually measured varies in constant relationship to the unavailable and unknown quantity being measured indirectly; and (2) other variables which change spontaneously or are induced by the procedure do not modify this relationship.[10]

Nitrous oxide method: A short time following the symposium on the cerebral circulation, Kety[16] conceived and subsequently developed a method which has made possible the quantitative measurement of cerebral blood flow and cerebral metabolism in intact man.[13] This is now known as the nitrous oxide method. This method involves the inhalation of a mixture of 15 per cent N_2O, 21 per cent O_2, and 64 per cent N_2. Blood samples are collected simultaneously from an artery and the superior jugular bulb; (1) during the first minute of inhalation, (2) at the end of the first minute, (3) the third minute, (4) the fifth minute, and (5) the tenth minute. An analysis is made of the N_2O content in the blood. Cerebral AV O_2 differences are calculated from the O_2 content in samples of blood taken before inhalation and after five minutes of inhalation. The mean arterial blood pressure is also determined during the procedure. From these measurements the blood flow in cc./100 Gm. brain/min.; the O_2 consumption in cc./100 Gm./min.; and the vascular resistance can be calculated.

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1. Sayer, R. J., et al.: Am. J. M. Sc. *221*:256 (Mar.) 1951.
2. Welch, H.: Ann. New York Acad. Sc. *53*:253 (Sept.) 1950.
3. Werner, C. A., et al.: Proc. Soc. Exper. Biol. & Med. *74*:261 (June) 1950.
4. Wolman, B., et al.: Brit. M. J. *1*:419 (Feb. 23) 1952.
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6. King, E. Q., et al.: J. A. M. A. *143*:1 (May 6) 1950.

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upon the cerebral blood flow and metabolism of the many drugs, hormones, nervous stimulation, hyperventilation, anoxia, and surgical procedures (i.e., carotid ligation) with a reasonable degree of accuracy.

N_2O method:[20] 1. Values for cerebral blood flow per 100 Gm. of brain, arterio-venous O_2 difference, A-V glucose difference, cerebral O_2 utilization, cerebral glucose utilization, and cerebrovascular resistance are given in 29 observations on 23 patients with cerebral vascular disease. The subjects were either middle aged persons with hypertension and diabetes or patients with a history of a CVA. They were divided into those with normal and those with abnormal mental status.

2. Those patients who had no alteration in their mental status had significantly lower cerebral blood flows, higher AV O_2 differences, and higher cerebrovascular resistances than normal young persons. Cerebral O_2 and cerebral glucose utilizations were normal.

3. The subjects with abnormal mental status resulting from cerebral vascular disease had significantly lower cerebral blood flows, cerebral O_2 and glucose utilizations, and higher cerebrovascular resistances than those with normal mental status or than normal young subjects.

4. It is believed that these groups represent two stages in the natural progression of cerebral vascular disease.

5. Unilateral stellate ganglion block produced no change in cerebral metabolic functions in normals, patients with hypertensive vascular disease, and elderly patients with cerebral thrombosis.

It is logical to assume that the reduction in blood flow is the result of diffuse vascular disease and not hypertension per se, since Kety and colleagues[14] have shown that in uncomplicated hypertension the cerebral blood flow and AV O_2 difference are normal though the cerebrovascular resistance is increased.

The decrease in cerebral metabolism is related to the inability of the brain cells to extract more O_2 and glucose per unit of blood, rather than to the low blood flow itself. This poor cellular function results in some way from the progressive vascular disease. Several possibilities exist, i. e.:

1. Insufficient areas of softening and scarring may have occurred so that part of the blood supply to the brain passes through areas of scar tissue.

2. Marked disturbances in function of uninjured cells may have resulted from the great disorder in total brain function produced by many local lesions.

3. In certain areas metabolism of existing cells may be greatly deranged by reductions in cerebral blood flow to a level incompatible with normal function but not sufficient to cause death.

4. Infection and altered metabolism in other organs may secondarily affect brain metabolism.

Arteriographic demonstration of arterial spasm:[5] By means of comparative arteriograms, they demonstrated arterial spasms (in vessels with interior diameter at least 1.5 mm.) in 12 instances among 10 cases. Vessels involved were internal carotid, anterior cerebral, middle cerebral arteries, and their branches.

The common element in the production of spasm in all cases seemed to be abrupt traction on the arterial wall, i.e. from association with aneurism, hemorrhage (local), edema, tumor, and severe intrinsic lesion of the arterial wall.

Usually spasm was maximal at the lesion but extended several centimeters along adjacent arteries in lesser degree.

V. CEREBRAL ANGIOSPASM

From a clinical standpoint, the physician over a period of years will see and treat a considerable number of patients with cerebral attacks. These attacks, of course, are characterized by a variety of symptoms depending upon the underlying pathology. The symptoms of cerebral hemorrhage and cerebral thrombosis are often quite obvious and the gross pathology quite evident.

There are, however, other types of cerebral attacks of a lesser degree in which the disturbances are of a much shorter duration, transient disturbances with perhaps no residual, in which the gross appearance of the brain after death is less noticeably altered.

It is with these transient episodes that we are here concerned. Even more specifically we are concerned with the question of whether or not cerebral angiospasm, per se, can and does produce these episodes. This may or may not seem a moot point, depending upon one's views. However, considering the fairly widespread acceptance of the idea of cerebral angiospasm, especially prior to World War II, and considering the experimental advances in studying cerebral circulation and the trends of thought since this time, his point is here thought to be worthwhile.

Pickering's excellent paper in 1948 on transient cerebral paralysis[19] describes encephalopathy in acute hypertension, in chronic hypertension, and that in cerebral embolism. He presents 22 cases of cerebral attacks, 11 of which showed transient motor or sensory paralysis of cerebral origin in essential hypertension, and 11 cases of cerebral embolism in mitral stenosis and auricular fibrillation. He points out the close similarity clinically and pathologically between the attacks in the two conditions and suggests a corresponding similarity in the underlying vascular events. In each instance the onset of the attack is due to organic arterial obstruction of sudden development and resolution due to restoration of circulation through dilatation of collateral vessels. The obstruction in one case is due to an embolus and in

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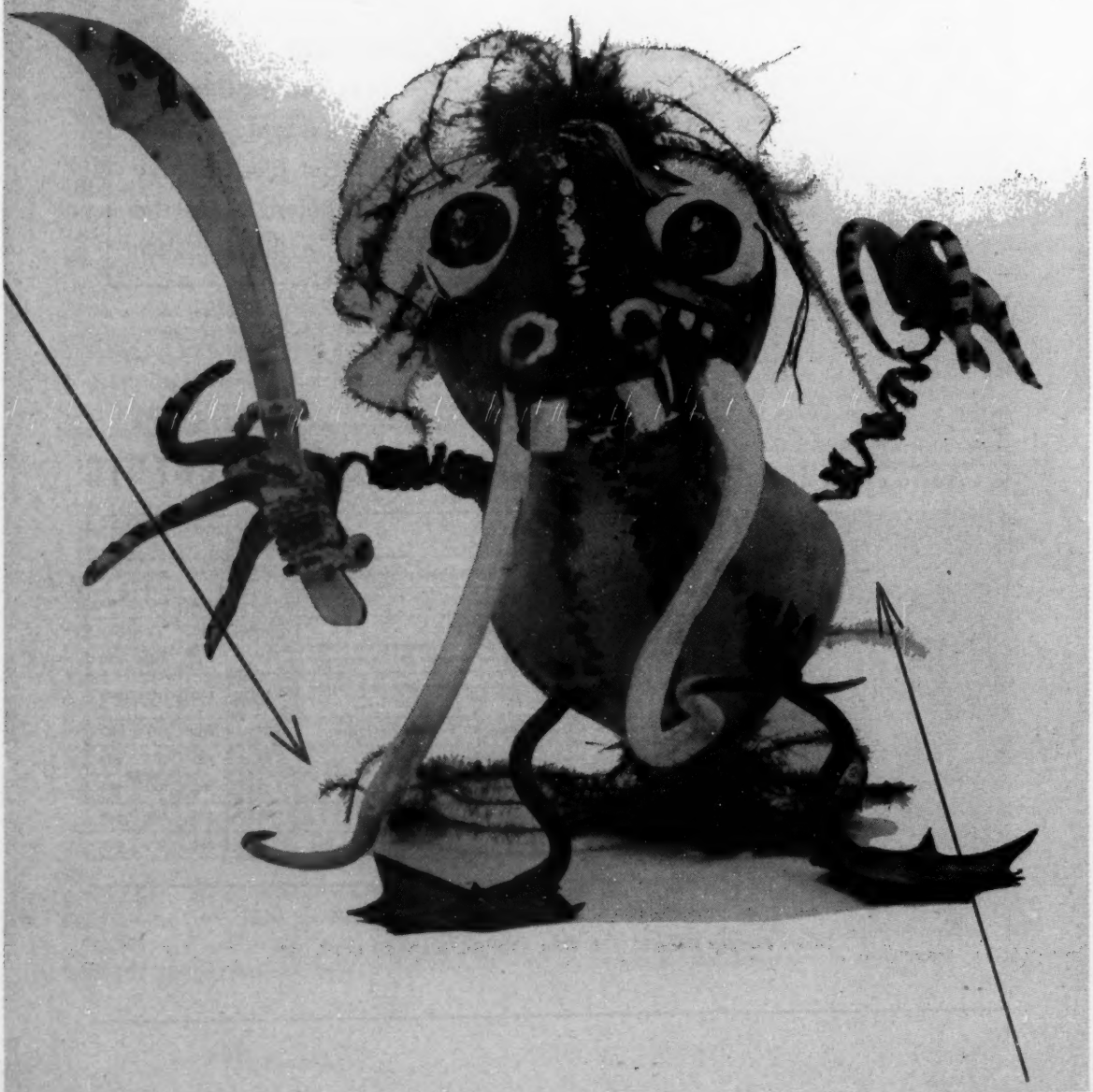

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1. Grigsby, M. E., et al., Antibiot. & Chemother., 10:1029, October, 1953.

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the other to thrombus formation. He attributes acute hypertensive episodes to cerebral edema as a result of defective vasoconstriction.

Latham[18] has demonstrated microscopic cerebrovascular lesions in a variety of organic diseases where the large vessels may not appear enlarged, and he points out Biggart's dictum: "The naked eye appearance of the larger vessels is no criterion of the presence or absence of vascular damage."

Kety[13] states that it is possible that reflex cerebrovascular spasm might occur in response to embolism or thrombosis and suggests that in that type of carotid sinus syndrome which produces syncope without a bradycardia or a fall in blood pressure an intense vasoconstriction might be produced, an exaggeration of the normal response. "Indeed, the entire question of cerebrovascular spasm to a degree sufficient to embarrass the cerebral circulation is a problem which requires much further investigation."

Schmidt[23] believes that while the possibility of cerebral angiospasm cannot be denied, the evidence is greatly against it.

Scheinker[21] states in regard to cerebral angiospasm: "Clinically it is not whether angiospasm can and does occur, but whether it is of significance to induce a variety of clinical manifestations. There is no direct or indirect proof that angiospastic phenomena are of paramount significance in migraine, epilepsy, hypertension, multiple sclerosis, etc. That spasm of an individual blood vessel is ever of sufficient intensity and duration to induce permanent damage to the tissue it supplies is questionable. It is to be little doubted that vascular dilatation to an extreme degree, in association with stasis, is by far the most striking and essential feature in such forms of functional vascular disturbances as vasoporosis, vasoparalysis, and vasothrombosis. The vasoparalytic dilatation of a cerebral blood vessel results in a retardation in cerebral blood flow, and there is every indication that the margin of safety of the nerve parenchyma is much smaller than that of any other organ, with regard to volume of blood per unit of time and percentage of O_2 carried by the blood. An extreme vascular dilatation, associated with stasis and retardation or cessation of blood flow, will thus result in an interference of O_2 and CO_2 exchange and affect tissue function."

Scheinker supports the idea of vasoparalytic phenomena possibly preceded by brief angiospasm. Transient clinical symptoms, such as hemiplegia and aphasia, do not rule out small focal areas of tissue destruction.

Clinically it might be said that transient cerebral attacks might well be a warning to the physician to consider other pathology before ascribing them to "angiospasm" per se.

VI. SUMMARY

1. The cerebral circulation is discussed from the standpoint of anatomy (both gross and microscopic), physiology, and recent experimental developments.

2. The subject of cerebral angiospasm is considered.

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Regional Meeting on Veterans' Care

A series of regional conferences on veterans' medical care will be held during 1954 under the sponsorship of the A.M.A.'s Council on Medical Service. The meeting for this area will be held at Denver on February 21.

These meetings have a fourfold purpose: (1) develop a working liaison with state society committees concerned with veterans' problems; (2) acquaint an increasing number of physicians with A.M.A. policy and the facts regarding veterans' care; (3) learn the local situation regarding this policy in various states, and (4) discuss ways of carrying out the instructions of the House of Delegates which adopted a firm stand on veterans' medical care at its meeting last June.

It is not too early to make hotel reservations for the 95th annual session, Kansas Medical Society, Topeka, May 2-6, 1954.

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An "extra large" four-day sectional meeting of the American College of Surgeons, featuring clinics and specialty programs, will be held at the Hotel Fontenelle in Omaha, March 1-4. All members of the medical profession are invited to attend.

The Foundation of the American Society of Plastic and Reconstructive Surgery announces an essay contest in two divisions, for those who are residents or who have practiced plastic surgery for no longer than five years and for those who have been active in the specialty for more than five years. Manuscripts will be accepted until July 1, 1954. Complete information may be secured from the Award Committee, c/o Jacques W. Maliniac, M.D., 30 Central Park South, New York, New York.

The Sixth Annual Symposium on Recent Advances in the Study of Venereal Diseases will be held in the auditorium of the Department of Health, Education, and Welfare, Washington, D. C., April 29 and 30. Sessions are open to all physicians interested in participating.

All physicians are invited to attend the Sixth Annual Convention of the International Academy of Proctology to be held at the Palmer House, Chicago, April 8-11. Much of the program has been planned to answer questions of general practitioners, gastroenterologists, and proctologists. There is no fee for attendance. Programs are available from the Executive Office of the Academy, 43-55 Kissena Boulevard, Flushing, New York.

The National Foundation for Infantile Paralysis announces the availability of a limited number of postdoctoral clinical fellowships in physical medicine

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WILLIAM M. BUSCH, LL.B., Business Manager and Attorney, Kansas State Board of Health, Topeka.
DONALD A. DUKELOW, M.D., Consultant in Health and Fitness, Bureau of Health Education, American Medical Association, Chicago, Ill.
THOMAS R. HOOD, M.D., Executive Secretary, Kansas State Board of Health, Topeka.
HARLAN R. SCHUYLER, M.S., Ph.D., Entomologist; President of Conservation Industries, Kansas City, Kans.
GEORGE M. WHEATLEY, M.D., Vice-President in Charge of Health and Welfare, Metropolitan Life Insurance Company, New York City.

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The Local Health Officer and Problems in Sanitation.
Health Is Everybody's Business.
A Croaking Frog and Three Mad Foxes.
International Control of Disease as It Affects the Local Health Officer.
Health Hazards of Insecticides and Rodenticides.
Toxoplasmosis.
Infectious Hepatitis.
The Physician and Child Health Services.
Needs of Children Today for Hospital and Health Services.
The Physician and the Schools.
Present-Day Concepts of Communicable Disease Control.
Comprehensive Medical Care for Children (a Panel Discussion).
Retrolental Fibroplasia; New Developments in Etiology and Prevention.
Etiologic Factors in Enteric Infections.
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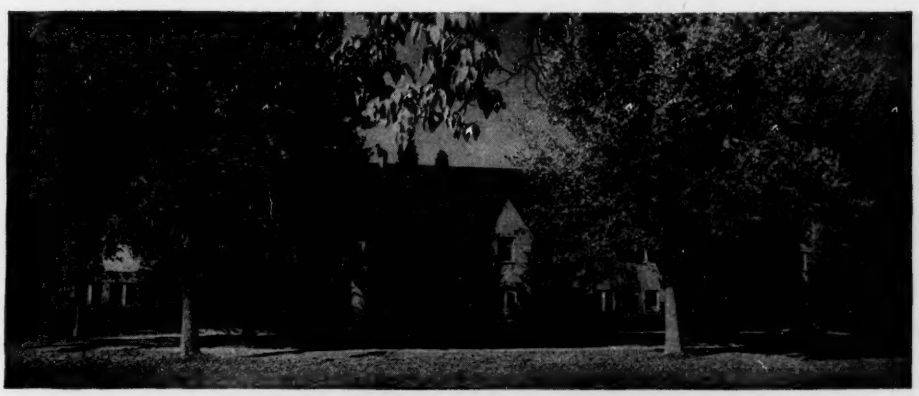

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The 1954 meeting of the American Goiter Association will be held at the Somerset Hotel, Boston, April 29-May 1. The three-day program will consist of papers and discussions dealing with the physiology and diseases of the thyroid gland.

The National Gastroenterological Association announces that the name of its official publication, established in 1934, has been changed from *The Review of Gastroenterology* to *The American Journal of Gastroenterology,* effective with the January issue. The current issue is Volume 21, Number 1.

Physicians are invited to attend the Sixth Congress of the Pan-Pacific Surgical Association to be held in Honolulu, October 7-8, 1954. The scientific program, presented by more than 100 surgeons, will include sessions in all divisions of surgery and related fields. A social program is being developed for the doctors' families. Complete information may be secured from F. J. Pinkerton, M.D., Director General, Pan-Pacific Surgical Association, Suite Seven, Young Building, Honolulu, Hawaii.

Grant to Committee on Careers in Nursing

A March of Dimes grant of $47,690 will assist the Committee on Careers of the National League for Nursing to continue its national program of recruitment of students for schools of professional and practical nursing.

Since 1949, the Foundation has provided financial assistance. The 1954 grant will underwrite the committee's field services program designed to help state and local committees in their efforts to interest young people in nursing careers.

Contributions to the American Medical Education Foundation during the first 11½ months of 1953 totalled $1,047,000. More than 24,500 physicians contributed $847,361 directly to 70 of the nation's 79 approved medical schools.

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The eventual goal of the study is to develop means of counteracting abnormal body processes, thus preventing or controlling disease.

The Motion of the Heart

A book commissioned by the American Heart Association and designed for a lay audience, "The Motion of the Heart," was published by Harper and Brothers on February 3. It describes the methods, objectives, and accomplishments of cardiovascular research. Mr. Blake Cabot wrote the book, which was reviewed before publication by Doctors Robert L. King, H. M. Marvin, Louis N. Katz, Howard B. Sprague, and Irving S. Wright.

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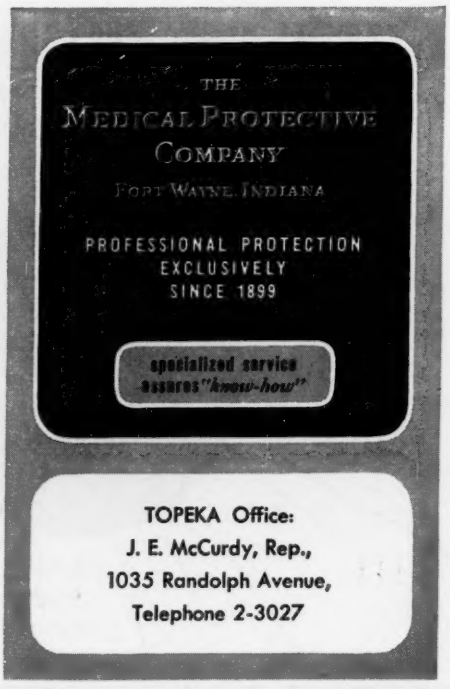

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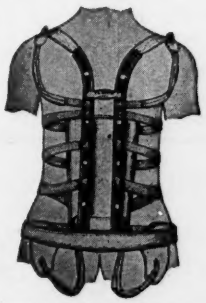

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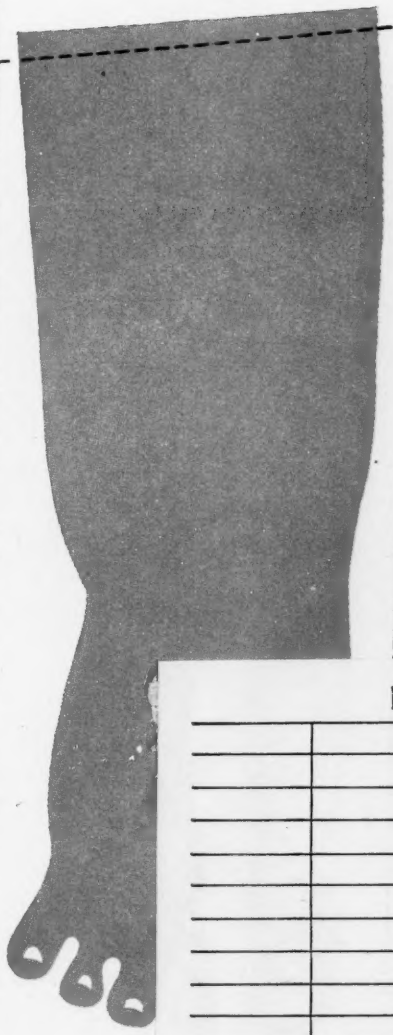

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